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FROM THE EDITOR

"It has been an enjoyable challenge to keep the doomsday specialists at bay – at least upto now."

Once again I pendown my thoughts about JK-Practitioner. The idea of producing an international specialist medical journal took place in the year 1994. Year 2002 marks the ninth year of non-stop publication. If you are familiar with the condition prevailing in this part of the globe, no doubt, you will also agree with me that the exercise has been daunting and demanding in all aspects. But it has been an enjoyable challenge to keep the doomsday specialists at bay -- at least upto now.

Our main aim was to present research taking place at our institutions in the state to the world and help update our doctors with vast expanding knowledge in the medical field. In many ways we have been successful. Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Govt. Medical College, Srinagar, Govt. Medical College, Jammu and other medical institutions of the country provide the bulk of the articles. Some of the issues tackled in these pages may not hold prime importance to the western community, but these issues we cannot ignore here.

I am thankful to our friends and well wishers abroad, who have helped us in maintaining international image of the journal. Their constant encouragement and "always ready to help attitude" has been a source of inspiration. We will not let them down.

I must thank our reviewers who have been helping us for what finally goes into print. My thanks to the excellent team we have been able to put together all these years, who make this quarterly event happen.

Suggestions from our readers and subscribers are welcome.
Wishing all a happy 2002.

Prof. GM Malik
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NATURAL HISTORY OF HEPATITIS C VIRUS INFECTION - RISK FACTORS FOR DISEASE PROGRESSION (PART II)

S.K. Sarin; D. Kapoor

Factors affecting progression of chronic Hepatitits C

As already mentioned, the rate of progression of disease following HCV infection is highly variable, in part due to various agent and host factors. Some of the important factors are discussed below (Table 10).

Table-10: Variables affecting the outcome of chronic hepatitis C virus infection

Host	Viral	Co-factors	Miscellaneous
Age*	Vira load	Alcohol*	Initial histology*
Race	Genotype	HBV*	Antiviral therapy*
Gender*	Quasispecies	HIV"*	
Immune response	Comorbid conditions		
HFF gene	(Haemodialysis haemophilia, thalassaemia etc.)		

** Well established variables*

Age and gender

Numerous studies have shown that older age and male sex are predictive of a greater chance to progression to cirrhosis in chronic hepatitis C. The older age may indirectly be a reflection of a longer duration of infection with HCV. Mattson et al.[29] noted that out of 92 patients with CHC, 64% of patients above 30 years of age had CAH while only 33% of those younger than 30 years had this lesion. Wejstal et al.[9] reported in their series of 127 patients that the mean age of patients with CPH was 29.7 years while that of patients with CAH or LC was 46.8 years. The mean time to LC after blood transfusion in the EUROHEP study[27] was 5.7 years in those >50 years of age and 15.8 years in those ≤50 years. However, the survival in the two age groups was not statistically different. The benign outcome of HCV infection in young female patients from the large, retrospective-prospective immunoglobulin studies has already been alluded to[14,15].

In a well designed analysis of progression of liver fibrosis in CHC patients, Poynard et al.[30] showed that only three independent factors were associated with an increased rate of fibrosis: age >40 years, male sex and daily alcohol consumption >50 g. According to them, the rate of fibrosis progression per year was 0.091 in those ≤20 years and 0.333 in those >50 years, thus implying progression to cirrhosis in 44 years and 12 years in the two groups respectively. The fibrosis progression in female patients was 0.111/year and in males, 0.154/ year, with the two groups of patients expected to reach the stage of LC in 36 years and 26 years respectively (Fig. 3).

The two parametes, sex and age, were used to calculate the probability of progression to LC from CHC in the back-calculation model by Deuffic et al.[5] They showed that at any age the annual probability of progression to cirrhosis is 10 times greater for men than women. For men aged 61-70 years this probability is 300 times greater than that for men aged 21-40 years (Table 11).

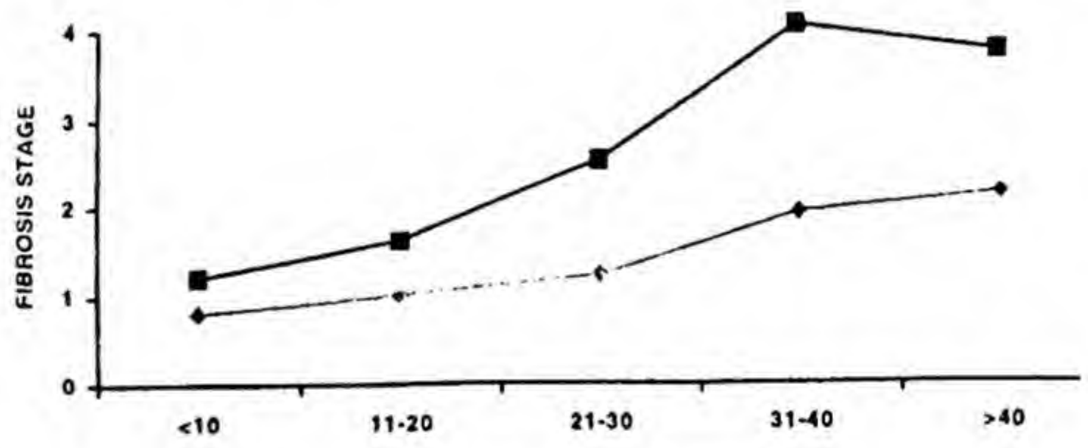

Figure 3: Association between fibrosis stage and duration of HIV Infection. Note the steep increase in the slope of the grap after 20 years of infection (Data from Ref. 30)

Table-11: Extimated clinical outcome in subjects infected with HCV at age 30 and 50 years[5]

	Age at infection (Years)	Percentiles in men			Percentiles in women		
		10	50	90	10	50	90
Time to cirrhosis (years)	30	22	32	42	27	44	55
	50	3	13	22	11	25	36
Time to HCC (yeas)	30	26	39	50	31	47	58
	50	8	19	30	15	29	40
Time to death from HCC	30	28	41	53	33	49	60
(Years)	50	10	21	33	17	31	41

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Immune response

It has long been known that CTL response is quite vigorous in patients with CHC, in sharp contrast to patients with chronic hepatitis B. In spite of this, viral clearance occurs in only a small percentage of patients actuely infected with HCV. Missale et al.[31] studied 21 subjects with acute hepatitis C and followed them sequentially for 44 weeks. Twelve patients normalized their ALT and 10 of these also became HCV RNA negative. The T-cell proliferative response to core, E2, NS3, NS4 and NS5 recombinant antigens and synthetic peptides was more vigorous and frequently detectable in this subject of patients rather than in nine patients who failed to normalize ALT or clear the virus. Thus, these early responses are extremely crucial in viral clearance. The host immune response comes to the fore even at the stage of CHC, when patients are retreated with antiviral agents such as interferon (IFN). Lohr et al.[32] showed that T cells from 16 of the 24 HLA-A2-positive, but none of the six HLA-A2-negative patients with CHC lysed targets primed with antigenic peptides. The CTL frequency in patients who had sustained response to IFN was higher than that in non-responders. Thus, the host immune response is a key determinant of outcome after HCV infections.

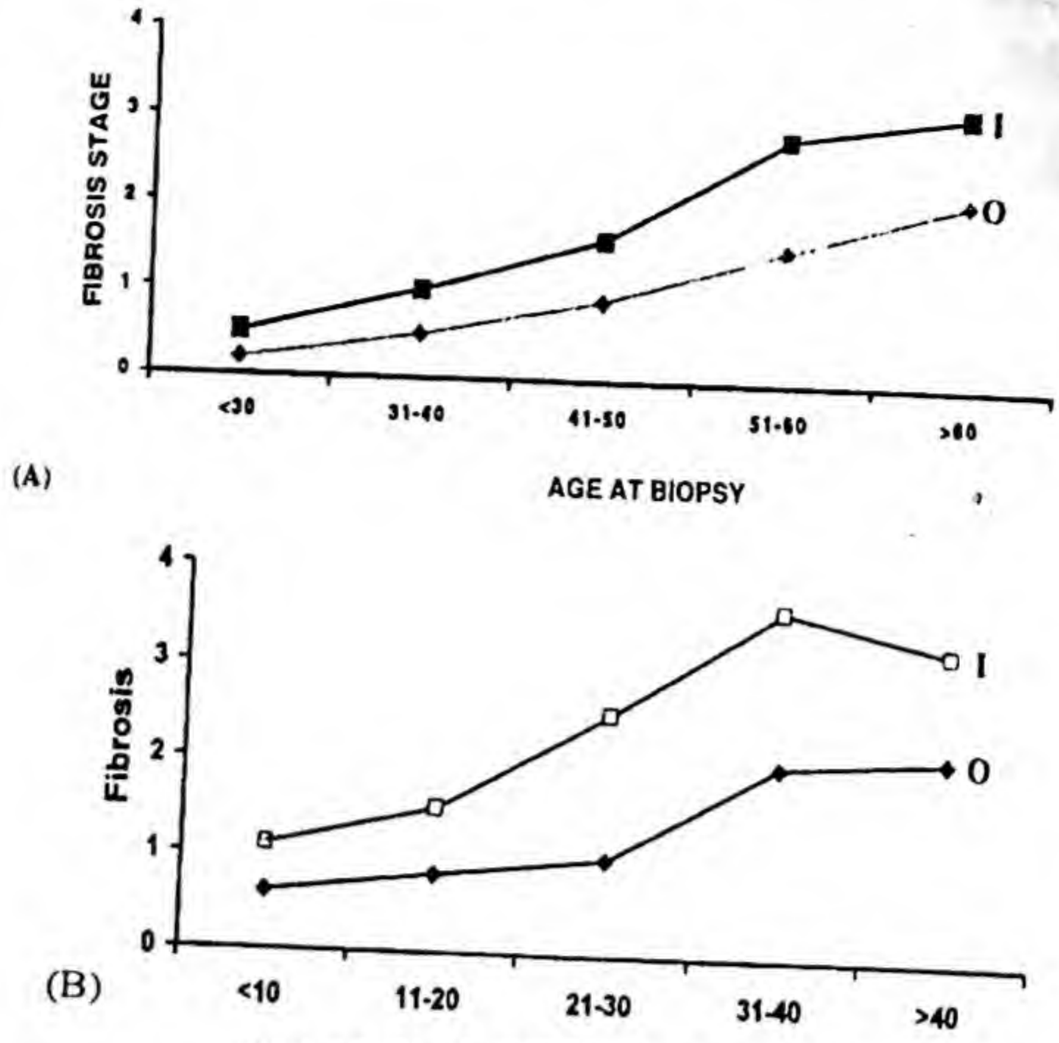

Figure 4: Association between fibrosis stage (A) Age at biopsy and (B) Duration of HCV infection in the presence (I) and absence (O) of alcohol. Note that alcohol consumption >50 g/day shifts the curve to the left (data from Ref. 30)

Viral factors

As has already been mentioned, the viral titres in a given patient with chronic HCV infection may remain steady over prolonged periods. Some authors have shown no correlation between the viral load and severity of liver disease[33] while others have observed a correlation between the height of viral titre and the stage of liver disease[34].

The influence of viral genotype on the outcome of chronic HCV infection is rather controversial: in most studies where genotype 1b was shown to be associated with more severe liver disease there were confounding factors like longer duration of infection, higher viral loads or studies being conducted at referral hospitals. Indeed, it has been shown that genotype 2 might be more prevalent in community and this genotype is associated with an indolent course of the disease[35]. Poynard et al. found no association between fibrosis progression and TV genotype[30]. Niederau et al.[26] also showed that the age, duration of infection, ALT levels and cirrhosis to be comparable in patients with genotype 1 and Genotypes 2 and 4 were associated with younger age of patients and shorter disease duration.

The association between genotype 1b and HCC is also equivocal, with some studies reporting a marginally increased relative risk[36], while others showed no other relationship[26,37]. The importance of HCV genotyping has gained recent interest, since results of large trials have shown that response to antiviral therapy better in non-1 genotypes[38]. The patients with other genotypes have a higher chance of attaining a sustained response and may be treated for even shorter periods (6 months).

The relationship between the degree of diversity of hepatitis C virus quasispecies 1 progression of liver disease is complex. Honda et al.[39] showed nucleotide diverging in the core and envelope region of the virus to steadily increase from stage of AH through CAH to LC. This intra-patient variation in nucleotides correlated with serum levels of ALT. However, such a correlation may not be really straightforward, as the circulating viral population may be different from the hepatic one and the latter which governs the extent of liver injury. Recently, Nagayama et al. also reported certain sequences of the HCV-Ib genome which may be related to progression of chronic hepatitis C[40].

Alcohol

Patients with alcoholic liver disease, the prevalence of HCVpositivity various from 15% to 35%, the serological test being more likely to be positve in those with severe histologic liver disease. Takase et al.[41] showed that the anti-HCV positivity was ~5% in patients with alcoholic fibrosis, 31% with cirrhosis 79% in those with HCC. HCV RNA is detected in about 95% of these anti-HCV-positive patients. In alcoholics, the possible routes of infections are the high behaviours like IVDA, sexual promiscuity or rarely, blood transfusion.

Cromic et al.[42] showed that after 4 months of alcohol-free diet, serum HCV A levels fell from 2.1 x 10^6 copies/

ml to 0.8 x 10^6 copies/ml in 15 patients who consumed <10 g/day of ethanol. The fall was more dramatic (2.6-0.42x/ml) in those inbibing 70 g/day of alcohol. Similar results were shown by pessione et al.[43] in a much larger study of 233 patients with CHC. In this study, RNA levels were three times higher in those consuming >210 g/day of alchol than in those not taking it.

Transaminase levels (especially ALT) are higher in alcoholics infected with HCV than in those seronegative for HCV. Also, the former group has a histologicallymore active disease (with respect to inflammation and fibrosis) and aphoid aggregates on liver biopsy in an alcoholic patient with liver disease point to concurrent HCV infection. Wiley et al.[44] showed that fibrosis progression in patients with HCV infection alone was lower (0.3±0.007/year) than those also consuming >40 g/day of alcohol (0.5 ± 0.13). In this series, the estimated incidence of cirrhosis in the 2 groups after 1,2,3 and 4 decades of follow up was 6% and 18%, 12% and 58%, 31% and 64% and 40% and 83%, respectively. Similar results were shown by Pyanard et al.[30] (Fig. 4). There is controversy regarding additive risk to development of HCC in HCV infected patients imbibing alcohol, but the bulk of current evidence does point to the synergistic effect.

Another impact of alcohol on outcome of CHC is the poor response to IFN, seen in patients consuming large amounts of alcohol. This might in part be due to the higher RNA levels seen in these patients (see above). Indeed Okazaki et al.[45] showed a lower sustained response to IFN therapy in those taking >60 g/day of alcohol.

HIV co-infection

Both HCV and HIV share the same routes of transmission and are common in those prone to high risk activities such as IVDA. Indeed, in the Euro SIDA cohort, of the 3048 HIV-positive patients, 33% were also anti-HCV positive and this proportion rose to 75% in those with history of IVDA[46].

HIV can accelerate the course of HCV infection, and in the series by Soto et al.[47] cirrhosis developed in 25% of HIV-postive IVDAs, in contrast to 6.5% of patients who were HIV negative. Serum HCV RNA levels are higher in these patients and tend to rise further as the CD43 counts fall. Over the last few years, with the use and success of highly active anti-retroviral therapies (HAART), the longevity of HIV-infected patients has increased, and in this new scenario HCV has emerged as a major cause of live disease-related morbidity and mortality in these patients. In addition, significant hepatotoxicity due to HAART may occur in patients co-infected with HCV, in part due to restoration of immune competence by these drugs and resultant hepatocytolysis in response to HCV infection in these patients[48].

The response to IFN in patients with HIV/HCV co-infection is similar to that seen in HIV-negative subjects with respect to end-of-treatment (ETR) response as well as sustained response (SR). However, the response rates tend to decrease with falling CD4+ counts[49]. Currently, trials are on to assess the response rate to combination therapy (IFN+ ribavirin) in these patients, but caution needs to be exercised in those receiving zidovudine (a nucleoside analogue which may cause bone marrow suppression) as it may accelerate the haemolytic anaemia caused by ribavirin.

HBV co-infection

Due to common routes of transmission, dual infection with HBV and HCV are frequent. Zarski et al.[50] compared 23 patients (HBsAg positive and anti-HCV positive) with 69 age- and sex-matched HBsAg-negative, anti-HCV-positive patients, HCV RNA levels were lower in members of the former group who were HBV DNA positive, thus implying inhibition of HCV replication by HBV in this group. The liver disease in the former group was histologically more severe with respect to cirrhosis, fibrosis, piecemeal necrosis and Knodell score.

The impact of dual infection on HCC is more controversial. Shiratori et al.[51] found dual infection in only 2% of 368 HCC patients vis-a-vis 1% of 119 patients with cirrhosis and 1% of 549 patients with CHC. In sharp contrast is the data of Kew et al.[52] from South Africa, who showed a relative risk for HCC of 23 in HBsAg-positive patients, 5 in anti HCV-positive patients but 82.5 in those with dual infection. Thus, in some geographical areas, the two viruses may have a synergistic role in disease progression.

Haemodialysis and renal transplantation

There is a wide range of reported prevalence of HCV infection in patients on maintenance hemodialysis (MHD). The seroprevalence of anti-HCV positivity in patients on MHD is declining but is still quite significant. As per the statement of European Dialysis and Transplant Association (EDTA), the prevalence declined from 21% in 1992 to 17.7% in 1993. In a recent study from Germany involving 2780 patients from 43 centres, HCV viraemia was seen in 3.7% of patients, representing a five times higher risk than in the general population[53]. About 18% of viraemic patients had normal ALT and/or anti-HCV negativity. This underscores the importance of a high index of suspicion and the need to use HCV RNA in addition to ALT and anti-HCV for testing these patients.

The risk factors for HCV infection among dialysis patients are;

i) Number of blood transfusions. Since the use of erythropoeitin and stringent screening of donor blood

this factor is becoming less important.

ii) Duration of dialysis. Even in those who have not received transfusion or have no history of IVDA or parenteral exposure, the prevalence of HCV infection with time has been shown to increase. Hardy et al.[54] found this rate of increase as 10%/year of MHD.

iii) Mode of dialysis. Patients on peritoneal dialysis are at a lower risk for HCV infection than those on MHD. In a group of 129 anti HCV negative patients on chronic dialysis, the seroconversion rate was 0.15% patient year in those on MHD and 0.03/patient year in those on peritoneal dialysis[55]. This may be because of lower transfusion requirement in the latter group, absence of vascular access site and extraocorporeal blood circuit in PD, and possibly most importantly, because peritoneal dialysis is a home procedure preventing the nosocomial transmission of HCV.

iv) Nosocomial transmission. This constitutes a major cause of HCV transmission in these patients. This may be because of a higher prevalence of HCV infection in dialysis staff which is, in turn, transmitted to non-infected patients. The staff may become infected by needle-stick injury from infected patients, breakdown in standard infection control practices and by physical proximity to infected patients. The role of dialysis machines, dialysis membrane and haemodialysis ultrafiltrate in infection is controversial. As regards reprocesing the dialysers, the risk of HCV transmission is not increased if dialysers from anti-HCV positive patients are processed in rooms different from those used for processing dialysers from uninfected patients.

It has been suggested that anti HCV+ve patients who undergo renal transplantations have an accelerated course. This may in fact be because of the immune depressed status of these patients and the use of immunosuppressive agents (like anti-lymphocyte and anti-thymocyte globulin, OKT3) in these patients, which causes increase in viral replication. The New England Organ Bank study[56] showed that anti-HCV positivity at the time of referral for transplantation was associated with increased mortality which was seen in patients who received a renal allograft or were continuing on dialysis. A more recent French study[57] with 29% of its 834 study subjects testing anti-HCV positive showed that the 5-year survival in those infected was not different from those not infected (85% vs. 87%), but at 10 years this difference became significant (65% vs. 80%). The infected group also had a lower graft survival. At 5 years the survival of those anti-HCV-positive subjects who had cirrhosis was similar to those who had lesser degrees of fibrosis, but at 10 years this difference became significant (33% vs. 69%). In those who had cirrhosis at the time of renal transplantation, the 10 year survival was a meager 26%. These authors thus support the view that all anti-HCV-positive subjects who are candidates for renal transplant should undergo a liver biopsy and presence of cirrhosis on histology should be a contraindication to transplantation.

Multiply transfused patients

The common categories of these patients are haemophiliacs, thalassaemics and those with hypogammaglobulinaemia. An elegant study from UK showed that mortality from liver disease in haemophiliac males was 16.7 times higher than that in the general population, and that from liver cancer was 5.6 times higher[58]. The risk of liver disease (including HCC)-related mortality increased with increasing age of first exposure to the blood products as well as concomitant infection with HIV. The same features apply to polytransfused thalassaemics, in whom the prevalence of HCV infection is quite high. Of the 75 thalassaemic children studied by us, anti-HCV positivity was seen in 68% cases[59]. Serum ferritin as well as ALT levels were higher in those infected than those who were uninfected. Indeed, iron may theoretically potentiate liver injury in this group of patients. Another interesting characteristic of the clinical course in this setting is the possibility of multiple episodes of acute attacks of hepatitis, possibly due to different genotypes[60].

In patients with congenital or acquired hypogammaglobulinaemia, use of contaminated intravenous immunoglobulin is responsible for high seroprevalence of HCV[61]. These patients often have biochemical and histological evidence of liver disease early in the clinical course. In the study by Bjoro et al.[62] nearly one-third of patients had histological evidence of cirrhosis which had developed 1-8 years following first exposure to contaminated immunoglobulins. These patients also face a management problem, as they show a poor sustained response to IFN therapy[63].

Initial histology and outcome of hepatitis C infection

A lot of recent work has highlighted the importance of liver histology early in the course of CHC as a prognostic factor for progression to more severe grades of chronic hepatitis or cirrhosis.

In the study by Di Bisceglie et al.[11] a second liver biopsy was performed in 20 of the 39 patients with chronic NANB hepatitis, about 8-26 months after the first biopsy (Fig. 2). The histology remained unchanged in nine, worsened in four (in three cirrhosis developed during this period) and improved in seven cases. Sanchez-Tapias et al.[64] found that in their study cohort of 306 patients, 7% of patients with CPH. 33% with moderate CAH and 47% of those with severe CAH developed cirrhosis after a mean of 8 years. Hopf et al.[65], in their study of 86 patients with post-transfusion or sporadic chronic hepatitis C infection followed for a mean of 8 years, found that none of the

patients with initial histological evidence of CAH moved to the stage of CPH or normal histology, but 53 of those with initial severe CAH progressed to cirrhosis. Similarly, Takahashi et al.[24] reported progression from stages of CPH, moderate CAH (CAH 2A) and severe CAH (CAH 2b) to LC after a mean period of 11, 9 and 7 years respectively.

In an elegant study by Yano et al.[66] 70 patients with chronic HCV infection underwent an average of 3.9 biopsies over a mean follow-up period of 8.8 years. The grade of initial biopsy was scored against a maximum score of 8(0-4 points for portal/periportal inflammation and 0-4 lobular inflammation) and the stage (signifying fibrosis) against a maximum score of 4 points. Overall, 35 patients (i.e. 50% of cases) progressed to LC. All patients with initial grade score $\geq$5 progressed to LC over 10 years; 96% of those with initial inflammatory score between 3.5 and 4.9 developed LC after 17 years and 30% of those with a score $\leq$3.4 developed LC after a mean of 13 years. Similarly, all patients with initial stage of septal fibrosis with incomplete nodularity (score 3-3.4) progressed to LC over 10 years.

The foregoing account lends credence to the observation that chronic HCV infection follows a rapidly progressive course in a subset of chronic hepatitis C, especially if the initial histological lesion is already significant.

IFN therapy and the outcome of chronic HCV infection

From the discussion thus far, it is amply clear that both necroinflammatory changes and fibrosis on liver histology determine the progression to cirrhosis in patients with CHC. So, it would be logical to assume that antiviral therapy which ameliorates these events should have a salutary effect on disease outcome. This beneficial effect of IFN is also noted in patients with dual infection due to hepatitis B and C[67].

The effect of IFN therapy can be broadly classified into:

1. Effect on fibrosis: A number of studies have addressed this issue. Suou et al.[68] showed a decrease in levels on N-terminal propeptide of type III procollagen (P-III-NP) in 178 patients treated with IFN-alpha. This effect was seen in patients who had a sustained or a non-sustained response to therapy and lasted for at least 1 year. No change in the levels of P-III-NP were seen in the 45 untreated patients. The decrease was also seen to be independent of the biochemical response.

   Manabe et al.[69] showed decrease in total liver collegen content by a colorimetric method in those treated even with 1 MU of IFN. In those treated with placebo, the collagen content increased. Similar results were shown by Hiramatsu et al.[70], who showed a beneficial effect on necro-inflammatory activity too (in addition to fibrosis), the patients losing HCV-RNA standing to gain the most from therapy.
2. Effect on cirrhosis: The results of two major studies[27,28] have already been mentioned elsewhere in this review. In the study by Fattoviich et al.[27] benefit from IFN therapy on survival was significant only on univariate analysis. Serfaty et al.[28] showed beneficial effect of IFN therapy on survival, hepatic decompensation and development of HCC on both univariate and multivariate analysis.
3. Effect on HCC: Two large multicentric studies have addressed this issue: The International Interferon Alfa Hepatocellular Carcinoma Study[71] and the Inhibition of Hepatocarcinogenesis by Interferon Therapy (IHIT) study[72]. In the first of these studies, 943 patients with biopsy proven cirrhosis were either treated with interferon (n=380; 42%) or followed without treatment (n=533; 58%). Each patient was followed for a period of at least 3 years. Although the study enrolled patients with both HBV and HCV related LC, only results on the subset of patients with HCV infection will be discussed. the authors found that significant risk factors for the development of HCC were age, male sex and features of portal hypertension. When all patients who were anti HCV positive were analysed with respect to development of HCC, that 48 of the 259 (18.5%) untreated and 21 of the 232 (9.1%) treated patients developed HCC (RR; 3:14; 95% CI: 1:09-3.64). In the subset of patients who were anti-HCV positive and anti-HBc-negative, the results were even more surprising: 29 of the 129 untreated (20%) and 6 of the 116 treated (5%) developing HCC (RR 6.28; 95% CI 1.65-23.8). The authors found that iron stores, alcohol intake, fibrosis stage and inflammatory grade had no effect on the outcome. Overall, only 15% of the study subjects showed a sustained virological response.

   In the much larger IHIT study[72] involving 2890 patients, 2400 patients received treatment with IFN and 490 were followed without treatment for a mean follow-up period of 4.3 years. The response to therapy was measured as biochemical and virological response and correlated with the fibrosis score at the initial histology. The risk of development of HCC was significantly reduced even in patients in whom there was no sustained virological response and only a biochemical response was achieved. The results of this study are shown in Tables 12 and 13. These studies drive home the point that IFN therapy even at the stage of compensated LC can significantly mould the outcome of chronic HCV infection, the factors leading to favourable outcome being anti-inflammatory and anti-fibrosis potential of IFN. There may be some other as yet unidentified mechanisms too. Why the same effects do not translate into benefit with respect to HCV development in patients with HBV related cirrhosis, is a still debatable issue.[71]

This review has systematically tried to highlight the

known facts regarding the natural history and course of HCV infection. It is appropriate to change the term HCV carrier to chronic HCV infection to highlight the ongoing hepatocellular injury. However, in spite of extensive research going into the mechanisms of disease caused by this agent discovered only a decade ago, the lacunae in our knowledge of the same are many. The complexities of host, agent and comorbid factors prevent any simple conclusions to be drawn and much effort needed in future to unravel the engima of HCV.

Table-12: Results of inhibition of hepatocarcinogenesis by interferon therapy (IHIT) study[72]

	Patients with sustained virological response (n=789)	Patients with nonsustained virological response (n-1568)
Normal ALT	724 (91.7%)	260 (16.6%)
ALT <2 x ULN	59 (7.5%)	592 (37.8%)
ALT >2 x ULN	6(0.8%)	716 (30.6%)
No. of HCC	10	76
Risk Ratio for HCC* (overall)	0.197 (p<0.001)	0.631 (p=0.016)

** Risk ratio for HCC: 145 events - 86 in the treated group and 59 in untreated group (see text)*

Table-13: Risk factors for development of HCC: multivariate analysis[72]

Parameter	Risk ratio	p
Sex (male vx. female)	1.551	0.012
Age (by every 1 year)	1.063	<0.001
Stage of fibrosis (compared with stage F0/F1)		
F2	4.43	0.002
F3	13.10	<0.001
F4	24.01	<0.001
Treatment with IFN 0.52	*<0.001*	

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PREVENTION OF VERTICAL TRANSMISSION IN HIV

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INTRODUCTION

- The term HIV refers to human immunodeficiency virus which belongs to the family of human retroviruses and subfamily of lentiviruses.
- There is a broad spectrum of HIV disease ranging from asymptomatic infection and clinical latency to advanced clinical disease the latter constituting AIDS.

Currently there are about five million HIV infected people in South East Asia. As of January 2000, over 135,000 cases of AIDS have been reported. In India 3,500,000 people are infected with HIV as on January 2000.[1]

DEFINING "AIDS" WHO clinical case definition[1] – Table 1

	Adults	Children
	At least 2 major + at least 1 minor sign in absence of known causes of immunosuppression (Ca/malnutrition) or other recognized etiologies.	At least 2 major + at least 2 minor signs in the absence of known causes of immunosuppression.
MAJOR SIGNS		
	(a) Weight loss > 1 mo. (b) Chronic diarrhea > 1 mo. (c) Prolonged fever > 1 mo.	(a) Wt. loss or abnormally slow growth/ failure to thrive >1 mo. (b) Chronic diarrhoea > 1 mo. (c) Prolonged fever > 1 mo.
MINOR SIGNS		
	(a) Persistent cough > 1 mo. (b) Generalized pruritic dermatitis (c) Recurrent Herpeszoster (d) Oropharyngeal candidiasis (e) Chronic progressive and disseminated *H. simplex infection.* (f) Generalized lymphadenopathy The presence of generalized Kaposi's Sarcoma or cryptococcal meningitis are sufficient by themselves for Dx of AIDS.	(a) Persistent cough > 1 mo. (b) Generalized dermatitis (c) Repeated common infections (otitis/pharyngitis etc.) (d) Oropharyngeal candidiasisd (e) Confirmed maternal HIV infection (f) Generalized lymphadenopathy

1993 Revised Classification System for HIV infection and Expanded Aids Surveillance Case for Adolescents and Adults.[2]

CD_4 C categories	Clinical Categories		
	A	B	C
	Asymptomatic, Acute (1°) HIV or PGL	Symptomatic not A or C	AIDS Indicator conditions
> 500/ml	A1	B1	C1
200-499/ ml	A2	B2	C2
< 200/ml	A3	B3	C3
A3 or B3 or C = AIDS			

WHO Clinical Case Definition for Southeast Asia (NACO, India)[1]

AIDS in adult diagnosed if meeting criteria **A and B**

(A) Positive test for HIV infection by two tests preferably based on two different antigens.

(B) Having one or more of
- (1) Wt. loss ³ 10%, not known to be due to a condition unrelated to HIV infection,
- (2) Chronic diarrhea > 1 mo., intermittent or persistent,
- (3) B/L Pulm T.B. or miliary or disseminated or extrapulm. T.B.,
- (4) Neurological impairment restricting daily activities, not known to be due to a condition unrelated to HIV (eg. trauma),
- (5) Candidiasis of esophagus,
- (6) Kaposi's Sarcoma

Principles of Laboratory Diagnosis of HIV infection[2]

(1) Detection of **specific antibodies**
- Screening test – ELISA
- Supplemental tests - IB (immunoblot)
  - WB (western blot)
  - IFA (indirect immunoflurescence)

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- RIPA (Radio immunoprecipitation assay

(2) Detection of **specific antigens**
- p24 Ag detection
- Reverse transcriptase assay

(3) Detection of **viral nucleic acid**
- in situ hybridization
- Polymerase chain reaction (genotyping/v. load assay)

(4) Isolation/culture of **virus** (syncytium inducing/non syncytium inducing)

(5) Indirect predictors of HIV infection (CD_4 count, serum neopterin, B_2 microglobulin, IL-2 receptors).

Therapeutic significance of these tests[3]

◆ 'Viral load' estimation (HIV RNA copies/ml blood) : Commonly available RNA PCR / bDNA test detect upto 500 copies/ml while newer ultrasensitive tests can detect upto 2 copies/ml.

◆ 'Negative' ultra sensitive tests do not mean a cure or clearance of HIV from blood. Low level replication persists with plasma RNA levels below detection levels in 'protected sanctuaries' (LNS, lymphatics CNS and tests). Also, the apparent decay half life of resting memory CD_4^+ cells with latent HIV provirus is upto 44 months and even longer. Therefore HIV eradication with presently available drugs is not a realistic goal HIV RNA level (viral load, VL) is the single best marker predicting the loss of CD_4^+ cells and clinical outcome. Other indicators are CD_4 count (CD_4C), biologic phenotype of virus, genetic polymorphism at CCRS HLA locus etc.

◆ VL has significance in
1. Dx or confirmation
2. Guide to start/stop/switch Tx
3. Assess risk of vertical transmission
4. Prognosis (VL > 10,000/ml + CD_4C > 500/mm^3 = 70% dead in 10 years)

ANTIRETROVIRAL THERAPY AND PREGNANCY[4,5,6]

Guidelines for optimal antiretroviral therapy and for initiation of therapy in pregnant HIV infected women should be same as those defined for non pregnant adults. Thus the woman's clinical virological and immunological status should be of primary importance in guiding its decisions.

WHEN TO START ANTIRETROVIRAL TREATMENT

Clinical category	CD_4 C+ VL	Recommendations
Symptomatic (AIDS)	Any value	Treat
Symptomatic	Acute 1° HIV infection (or < 6 mo. After seroconversion)	Treatment should be offered
Asymptomatic	CD_4 C < 500 or VL > 10,000	Treatment should be offered. Strength of recommendation based on prognosis for disease free survival and patients willingness
Asymptomatic	CD_4 C > 500 and VL < 10,000	Can delay therapy and observe.

One can face two situations :

(a) HIV positive women who are in first trimester of pregnancy and who are not receiving antiretroviral therapy may wish to consider delaying initiation of therapy until after 10-12 weeks of gestation since this is the period of organogenesis when embryo is most susceptible to potential teratogenic effects of drugs; the risk of antiretroviral therapy to fetus during that period are unknown.

(b) Some women already receiving antiretroviral therapy may recognize their pregnancy early enough in gestation that concern for potential teratogenicity may lead them to consider temporarily stopping antiretroviral therapy until after the first trimester. There are insufficient data to support or refute teratogenic risk of antiretroviral drugs when administered during the first 10-12 weeks of gestation. However, a rebound in viral levels would be anticipated during the period of discontinuation and this rebound could theoretically be associated with increased risk of early in utero HIV transmission or could potentiate disease progression in the woman. Although the effects of all antiretroviral drugs on the developing fetus during the first trimester are uncertain, most experts recommend continuation of a maximally suppressive regimen even during the first trimester. If antiretroviral therapy is discontinued during the first trimester for any reason, all agents should be stopped simultaneously to avoid development of resistance. Once the drugs are reinstituted, they should be introduced simultaneously for the same reason.

What is Vertical Transmission (VT)?

◆ VT refers to the transmission of infection from one generation to other i.e. from mother to child.

◆ HIV can be transmitted from an infected mother to her fetus during pregnancy or to her infant during delivery.

◆ This is very important mode of transmission of HIV infection in developing countries.

◆ 1600 infants acquire HIV infection everyday. HIV I transmission from an infected mother to her baby is estimated to be 21-43% in less developed countries with more than half of the transmission probably occurring late in pregnancy or during delivery.[7]

Maternal-infant transmission of HIV occurs in one of three ways : Intrauterine or intrapartum transmission, or postpartum transmission through breastfeeding. Each mode

has its own mechanisms, risk factors, and interventions. For each mode, the characteristics of the host (the mother), the recipient (the infant), and the virus may contribute to the likelihood of transmission.

PRESUMPTIVE EVIDENCE OF TIMING OF VT[2,8,9]

- As previously stated HIV can be transmitted from the mother to fetus during pregnancy as early as the first and second trimester. However maternal transmissions of fetus occur most commonly during perinatal period.
- Transmission during antenatal period is indicated by :
- Identification of HIV in aborted fetal tissue from infected women
- Presence of HIV in peripheral blood in 50% of infected infants in first week of life.
- Factors that indicate a very low antenatal rate of vertical transmission and predominant perinatal transmission include.
  - Appearance of HIV specific IgA antibody within 3-6 months after birth.
  - Appearance of p-24 antigenemia weeks to months after delivery but not at the time of delivery.
  - PCR assay of infant blood that is negative following delivery but positive several months later.
  - Cesarean section decreases transmission.
- Epidemiological data indicate that breast feeding is associated with an approximate doubling of HIV-I transmission risk but the proportion occurring during early and late breast feeding is not well defined.

Risk Factors for vertical Transmission

Various factors that affect the rate of transmission include :

Viral characteristics:[2,10,11]

- Amount of maternal viral load as reflected by
  - P-24 antigemia
  - HIV RNA levels[3]
  - HIV DNA levels
- Other factor which are assumed to reflect viral load indirectly include
  - Maternal CD_4 + T-cell counts
  - Advanced clinical disease
  - Increased plasma levels of
    - Neopterin
    - P_2 microglobulin

Pregnancy and Delivery

- Chorioamnionitis and other sexually transmitted disease are associated with disruption of placental barrier in pregnancy and premature delivery and with increased viral load in genital tract.
- Mode of delivery.[12,13]

Decreased likelihood of HIV transmission observed with elective caesarean section is related to avoidance of

- Microtansfusions of blood during labour
- Direct contact of fetus with maternal genital tract secretions or blood during parturition.

Risk of transmission is higher among women in whom labour beings, membranes rupture on both occur before a planned caesarean section can be performed.

(The benefit of elective cesarean section with regard to mother-to-infant transmission of HIV must be weighed against the possible deleterious effects of surgical delivery. Among women without HIV infection cesarean section has been associated with increased neonatal morbidity and maternal morbidity and mortality, as compared with nonsurgical delivery. The fetal or maternal indications for nonelective cesarean section themselves may be associated with postoperative neonatal or maternal morbidity. However, elective cesarean section is associated with a lower risk of maternal complications than is emergency cesarean section.

Previous reports indicates that HIV infected women have an increased risk of peripartum and postpartum infectious complications that are related to the level of immunologic deficiency and an increased risk of postoperative complications, including death, if they live in less-developed countries. In less-developed countries, the potential risks associated with elective cesarean section would appear to outweigh the potential benefit in terms of decreased vertical transmission of HIV).

- Duration of labour
- Interval from the time of membrane rupture to delivery
- Events during labour and delivery that can expose infant to mother's blood viz.
  - Abruption
  - Use of fetal scalp electrodes
  - Episiotomy
  - Severe lacerations

Infants :

- Gestational age at birth
- Birth weight
- Breaks in infant skin during labour

Postnatal transmission via breast feeding.[14]

- Viral load in milk
- Presence of mastitis

  Mastitis[15] leads to an opening of paracellular pathways with an increase in sodium, inflammatory mediators and inflammatory cells such as neutrophils and lymphocytes and plasma derived components that could contain HIV.
- Nipple pathology
- Variation in feeding practices

STRATEGIES TO REDUCE VERTICAL TRANSMISSION[7]

The strategies in use or under study for reducing the risk of maternal-infant transmission include the following, alone or in combination :

- Reducing the maternal plasma viral level systemically through the use of antiretroviral or immune therapy.
- Reducing the exposure of the infant to maternal blood and secretions (e.g., through delivery by cesarean section).
- Treating conditions that might facilitate transmission (e.g., through the use of antibiotics for chorioamnionitis).
- Reducing the viral level in genital secretions through the use of local agents, such as chlorhexidine.
- Treating the infant with antiretroviral therapy prophylactically or with hyperimmune globulin, monoclonal antibody, or HIV vaccination.
- Optimal obstetrical practices to prevent premature birth, rupture of membranes more than four hours before delivery, and the unnecessary use of instruments during delivery also probably reduce the risk of transmission.
- Postpartum transmission can be prevented by the avoidance of breastfeeding.

VARIOUS ANTIRETROVIRAL REGIMENS TO PREVENT VERTICAL TRANSMISSION

In 1994 a placebo controlled PACTG 076 showed that administration of zidovudine to mother during pregnancy and labour and to the infant for 6 weeks after birth was shown to reduce transmission. The doses were :

Antepartum : 100 mg orally 5 times daily starting at 14-34 weeks of gestation.
Intrapartum : 2 mg/kg intravenous infusion over 1 hr followed by continuous hourly infusion of 1 mg/kg.
Infant : 2 mg/kg orally four times daily for 6 weeks

The incorporation of this complex regimen[7] into clinical practice in the USA and other more developed countries coupled with increased prenatal HIV counseling and testing resulted in falling perinatal transmission rates to as low as 4-6%. The results of this trial are not directly applicable in developing country settings for the following reasons :

- Unknown efficacy of zidovudine monotherapy in pregnant females if breastfeeding cannot be discontinued.
- Need for early prenatal visits
- Need for frequent dosing
- Intravenous infusion during labour
- Administration 4 times daily for 6 weeks to babies.

The next breakthrough came with the results of Bangkok trial[16] (Thailand) and Ivory Coast Trial[17] which showed that short course zidovudine therapy[18] lowers the risk of VT by 50% in non breast fed and 39% in breast fed individuals. The regimen used was

Antepartum: 300 mg twice daily at 36 weeks of gestation
Intrapartum : 300 mg 3 hourly beginning from the onset of labour

Short course Zidovudine was :

- Simpler
- Cheaper
- Easy to administer

This regimen decreases viral load at delivery when there are maximum chances of transmission.

Next came the use of intrapartum and neonatal single dose Nevirapine.[19] It is a non nucleoside RTI which has a potent antiretroviral activity, is rapidly absorbed when given orally and passes quickly through placenta. This drug has a very long half life in pregnant women (61-66 hours) and babies (44-56 hours) which makes it an excellent candidate for use as a single dose intervention during labour. The regimen used was

Intrapartum : Single 200 mg oral dose at onset of labour
Infant : Single 2 mg/kg oral dose at age 48-72 hrs.

Most vertical HIV-1 transmission occurs during active labour because of maternal blood transfusions to neonates and direct exposure to the virus during passage through the birth canal. Therefore, maternal viral load must be substantially decreased by the time of labour or the baby must have systemic concentrations of active drug present at the time of HIV-1 exposure to successfully lower risk of transmission. Nevirapine[19] has several characteristics that distinguish it from zidovudine, which may explain why its use as an intrapartum and postpartum regimen is superior in lowering transmission risk. Unlike zidovudine.

- Nevirapine can decrease plasma HIV-1 RNA concentration by at least 1.3 log after a single dose.
- Is active immediately against intracellular and extracellular virus.
- Does not have to be taken up by the cell and metabolized to its active form. Therefore, nevirapine could be more effective than zidovudine when given close to the time of exposure, and may have had a more striking effect in decreasing viral load in colostrums and early breast milk samples.
- Nevirapine also has a long half-life compared with zidovudine and needs to be administered to babies only once to maintain a plasma drug concentration more than ten times the IC_{50} for 7 days.
- Furthermore, the variability of drug concentrations during the first week of life would be expected to be much less than that seen with zidovudine, which has a

short half-life and requires multiple dosing to maintain virucidal concentrations.

Therefore, maintenance of an effective prophylactic drug concentration during the first week of life, when additional HIV-1 exposure may occur through breast milk, may be important in explaining the relative efficacy of nevirapine compared with zidovudine in a breastfeeding population.

SAINT Study[20] (South African Intrapartum Nevirapine Trial) has very recently shown that a simple, inexpensive regimen of NVP (nevirapine) treatment given at the onset of labour can significantly reduce peripartum transmission of HIV-1 with an efficacy similar to a combination of ZDV and Lamivudine (3TC). On the basis of successful outcome of HIVNET 012 and SAINT Trial it is now being argued that in populations where HIV seroprevalnece is extremely high, it will be cost effective to treat all pregnant women and infants without prior counseling and testing with single dose of NVP.

A preliminary study found that 3 of 15 women receiving single dose NVP during labour had the K103 N NVP resistance mutation identified at 6 weeks postpartum. But clinical significance of this finding is uncertain. There is no evidence that NVP resistance accelerates progression of HIV-1 disease or increases transmissibility.[7]

Considering the simplicity, unmatched efficacy and low cost (around US $ 4.00 wholesale cost), NVP regimen is going to be one of the few deliverable and sustainable strategies for prevention of perinatal HIV-transmission in resource-poor setting. The challenge is to translate its utility into public health policy. It can reverse the dramatic trends of AIDS-related paediatric mortality.

Table : SAINT study regimens nterim analysis report

Treatment	During Labour dosing	During following labour dosing	Transmission rate*
NVP	200 mg single	Mother 200 mg single Infant 6mg single dose	14%
ZDV+3TC	ZDV-600 mg. onset then 300 mg/3 h 3TC-1500 mg. 12 times hourly	Mother ZDV-300 mg bd +3TC 150 mg bd for 1 wk Infant-ZDV- 12 mg bd+3TC 6 mg bd for 1 wk	10.8%

Without intervention transmission rate was 22-25%, with intervention reduction in transmission rate has been shown

POTENTIAL ADVERSE EFFECTS OF IN-UTERO AND NEONATAL ANTIRETROVIRAL EXPOSURE[7]

Short term data on zidovudine safety are reassuring. In PACTG 076 congenital abnormalities, preterm delivery and low birth weight were similar in zidovudine and placebo groups.

Although follow-up of antiretroviral exposed infants for long term toxic effects is a priority, current data indicate that if such effects are seen they are likely to be rare. Given the fatal nature of HIV infection, the risk of potential toxic effects is clearly outweighted by the proven benefit of reducing transmission by nearly 70% with the PACTG 076 regimen and 40-50% with short course antiretroviral interventions.

BREASTFEEDING AND VERTICAL TRANSMISSION[14,15,21]

Although most transmission of HIV occurs during pregnancy and at birth breastfeeding may account for 5-15% of infants becoming infected with HIV after delivery. In many countries where formula preparation is impeded by lack of clean water and proper hygienic, the nutritional and immunological benefits of breastfeeding are considered to outweigh the risk of mother to child transmission of HIV. The most important risk factors for vertical transmission are viral load in breast milk and presence of mastitis.

The vertical transmission of HIV through breast milk is dependent on the pattern of breastfeeding and not simply on all breastfeeding. Exclusive breastfeeding carries a significantly lower risk (almost half the risk) than mixed feeding.

Breast milk contains non-specific immune factors that have antiviral and anti-HIV-1 effects in vitro. These factors include :

- Secretory leucocyte protease inhibitor
- Lactoferrin
- Complement
- Glycosaminoglycan.

The finding that mixed feeding carried the highest risk is not surprising because the beneficial immune factors of breast milk are probably counteracted by damage to the infant's gut by contaminants or allergens in mixed feeds.

Breast milk contains growth factors, such as epidermal growth factor and transforming growth factor b, which may enhance the maturation of the gut epithelial barrier, thus maintaining its integrity and hindering passage of virus.

Ingestion of contaminated water, fluids, and food may lead to gut mucosal injury and disruption of immune barriers. Since mixed feeding is unlikely to involve hygienic food preparation practices, bacteria and other contaminants may be introduced into the gut and result in inflammatory responses and subsequent damage to the mucosa. HIV-1 is less likely to penetrate intact and healthy gastrointestinal mucosa than damaged mucosa.

Once the integrity of mucosal surfaces has been compromised by infection, allergens, or trauma, the passage of HIV-1 across mucous membranes into body tissues is facilitated. Early weaning is thought to retain the benefits of breastfeeding while lowering the risk of HIV-1 transmission. The best time for early weaning is 3 months. A possible recommendation is for exclusive breastfeeding with early weaning. In addition, the benefits of breastfeeding are particularly important in the first 3 months of life.

CONCLUSION[7]

Although significant progress has been made in the prevention of mother-to-child transmission, much remains to be done.

In the USA and other more-developed countries, where new perinatal infections are now rare, critical needs include the following :

- Identification of populations that do not receive HIV-1 testing or prophylaxis, and development of outreach programmes and effective interventions for these women;
- Establishment of the causes of prophylaxis failure, including the effect of evolving patterns of drug resistance on prophylaxis efficacy;
- Finding ways to further reduce transmission; and
- Evaluation of the potential short-term and long-term adverse consequences of in-utero antiretroviral exposure.

In less-developed countries, effective interventions have remained unimplemented, and economic and technical assistance for improving and strengthening the maternal and child health-care infrastructure and for developing implementation programmes is essential. Critical issues include the following :

- How to best accomplish HIV-1 counseling and testing in less-developed countries;
- Development of interventions applicable to even the most resource-poor nations, including those that permit maintenance of infant nutrition and health through breastfeeding while preventing postnatal transmission;
- Assessment of the morbidity and mortality associated with replacement feeding or early weaning in these settings.

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LASERS IN DERMATOLOGY

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INTRODUCTION

Ever since the original development of lasers by Maiman in 1959, they have been used in diverse fields ranging from missile technology to the different medical and surgical disciplines. In the field of dermatology,the use of lasers has been showing an increasing trend constantly over the last25yrs.Infact,the field of dermatological surgery has undergone a revolutionary change with the advent of lasers. With every passing day, more and more dermatological lesions are becoming amenable to treatment by lasers.

WHAT ARE LASERS?

Laser is basically a type of light or electromagnetic radiation which posseses certain special characteristics. Lasers are produced by a process known as "stimulated emmision of radiation".Infact, the word 'laser' itself is an acronym which means " Light amplification by stimulated emission of radiation". This process of stimulated emission can be explained as follows:

As is well known, electrons in a higher energy state are unstable and always tend to decay to a state of lower energy with spontaneous emission of energy(photons). Now, if a photon strikes an atom which is already in an excited state, the atom will decay to its ground state with release of two photons. In this process, these photons acquire certain special properties in the sense that they are of identical energy, frequency and wavelength and travel in the same direction and in phase with each other. If these two photons are made to strike two more atoms in an excited state, four photons possessing the same characteristic properties will be produced. This process can thus go on getting sequentially amplified provided the population inversion state is maintained by an external energy source. This amplification of light energy by " stimulated emission of radiation" is the basis for generation of laser energy(waves).

PROPERTIES OF LASERS

Laser light differs from ordinary light in a number of ways. Firstly, the laser light is always monochromatic i.e. the light from a given laser source has always a fixed, single wavelength. This is in contrast to the polychromatic nature of standard light with wavelengths ranging from 400 to 700 nm in the visible spectrum alone.

Secondly, laser light is also 'coherent' meaning that the waves of energy are in phase with each other both in space as well as time.Thirdly, laser light is always 'collimated' which means that the laser beam component waves are highly parallel producing a narrow beam that can be propagated for long distances with minimal divergence or convergence. This property of laser light is quite useful in focussing high power densities to small areas of human skin and other tissues.

COMPONENTS OF A LASER SYSTEM

All laser systems share certain basic components:

1. Laser medium- which is either solid(ruby crystal), liquid(rhodamine dye) or gas(argon).
2. Resonator or optical cavity- This is the sealed chamber which contains the laser medium.It possesses mirrors at either end which reflect the photon back to the medium for amplification to continue. The photons thus align themselves along the long axis of the chamber parallel to mirrors.
3. Energy source- This is needed to induce population inversion in the lasing medium. The different energy sources which are used include the standard AC power supply, radiofrequency waves, light energy etc.
4. Delivery system- This is a fibre optic system which brings the laser beam from the machine to the tissues.

TYPES OF LASER DELIVERY: CONTINUOUS V/S PULSED LASERS

The laser beam from a system can be emitted either in a continuous fashion or as short pulses. The delivery of laser light in pulses has a number of advantages over the continuous mode of delivery.By use of ultrashort pulses (of microsecond range) the thermal injury to tissues is minimized to a large extent as the tissues are allowed a

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cooling phase during the 'off' portion of the cycle. Some new laser systems even use pulses of the duration of nanoseconds e.g. the Q- switched laser.

LASER TISSUE INTERACTIONS

After an incident beam of laser light falls on the skin, it can either be reflected back or scattered within the tissues or can get transmitted through the skin or else it can get absorbed by the tissue itself. A biological effect is possible only in the last instance i.e. when the laser energy gets absorbed by a tissue component. The tendency of tissues to absorb this energy is wavelength dependent and can be measured by the absorption coefficient at that wavelength. Different tissue chromophores absorb energy at different wavelengths e.g. melanin absorbs energy specifically at 440 nm wavelength while hemoglobin preferentially absorbs energy at 577-585 nm wavelength. This property is used in the selection of lasers for different tissues and for different skin lesions.

APPLICATION OF DIFFERENT LASERS IN DERMATOLOGY

A large number of skin lesions are now amenable to treatment by lasers. These include vascular lesions like portwine stains, hemangiomas, pyogenic granulomas, vascular neoplasms etc ; pigmented lesions like melanocytic nevi, ephelides, tattoos and malignant melanoma ; hypertrophic or atrophic scars, wrinkles and perioral rhytides . Lasers are also nowadays being used in different dermatological applications/ procedures like hair transplantation, hair ablation by electrolysis, dermabrasion, photodynamic therapies and other such procedures.

Different laser systems which are used in dermatology and their application are discussed as under:

1. ARGON LASER

This was the first laser system used widely for treatment of vascular lesions. It gives a continuous wave emission of blue- green light with two energy peaks at 488 and 514 nm.[1] Clinically the laser energy is absorbed by corresponding chromophores i.e. either hemoglobin or melanin producing relatively localized thermal damage. As the treated area undergoes repair, fibrosis of vessels and target tissues results in gradual improvement of the skin lesions.

Cutaneous lesions which are treated by Argon lasers include: vascular lesions like portwine stains, angiofibromas, pyogenic granulomas, glomus tumors and pigmented lesions like lentigines, Nevus of Ota, ephelides, café-u- lait macules etc.[2]

Clinical fading of lesions takes around 4-6 months and side-effects encountered are pain and blistering which usually takes several days to resolve.[1]

2. TUNABLE DYE LASERS/ PULSED DYE LASERS

These laser systems generate energy at specified wavelengths of 577 nm and 585 nm – this allows for greater absorption of laser energy by hemoglobin as compared with melanin. Thus, these lasers are used preferentially for the treatment of different vascular lesions.[3]

Pulsed dye lasers emit energy in extremely short bursts of 300-500 u sec duration. High peak powers of short duration are thus produced which decreases the chances of non specific effect on surrounding tissues. The advantages with the use of pulsed dye lasers include less chances of scarring, reduced need for use of local anaesthetics and superior cosmetic results in vascular lesions.[4] Pulsed dye lasers leave a characteristic non blanchable purpuric area- this is used as the clinical endpoint of therapy.[3]

3. NEODYNIUM-YAG LASERS

This laser system produces energy in the near infrared portion of electromagnetic spectrum at 1060 nm. The energy is emitted from a solid YAG(yttrium-aluminium- garnet) crystal in the presence of Neodynium. There is no specific tissue chromophore for this laser and its main advantage is that it achieves a very deep penetration as compared with other lasers. It is thus useful in the treatment of deep vascular neoplasms, subcutaneous lesions like deep cavernous hemangiomas etc.[5]

The emission from an Nd- YAG laser can also be directed through a doubled crystal to produce a laser beam of wavelength 532 nm- this is known as the frequency doubled Nd- YAG laser. The treatment with this laser is claimed to be less painful and also produces less tissue reaction as compared to Argon lasers. [6]

4. RUBY LASER

This was the first clinically applicable laser system developed by Maiman in 1959. It uses a solid ruby crystal as laser medium and a pulsed red colored light with 694 nm wavelength. Absorption by tissues is somewhat nonspecific- however the laser has been successfully used in the treatment of melanocytic nevi and in removal of tattoos.It has been claimed that the blue-black pigmented tattoos respond best to treatment by this laser.[7]

5. CARBON DIOXIDE LASER

This is one of the most versatile lasers available, being useful in a number of dermatological procedures. The wavelength of the CO2 laser is 10,600 nm i.e, in the far

infrared spectrum. Water has a high absorption coefficient for light of this wavelength. Therefore the great majority of the incident beam's energy is absorbed in a depth of only 0.1 mm of soft tissue with minimal reflectance or scatter.

There are two fundamental methods of operation of the CO2 laser- the vaporization method and the incisional method. The former method is used in removal of relatively broad, shallow areas of tissue.Any lesions that can be treated with standard dermatological methods like electrosurgery, curettage or cryosurgery, are now amenable to treatment with CO2 vaporization. The ability of the laser to seal small blood vessels also gives a bloodless field with excellent visualization of the tissues. The ' noncontact' nature of laser surgery also gives the advantage of a more sterile field.

Thus the lesions amenable to treatment by CO2 vaporization include syringomas, trichoepitheliomas, superficial basal cell carcinomas, Bowen's disease, Condylomas, verruccae , angiofibromas, actinic cheilitis, rhinophyma etc.[8]

The incisional mode of CO2 laser is used as a cutting surgical tool in different dermatological surgeries like Moh's micrographic technique, blepharoplasty,etc. Any lesion amenable to cold steel surgery is a candidate for CO2 laser with the added advantage of being useful in patients with coagulation abnormalities, hypertension and patients with pacemakers[8].

In the recent times , ultrapulser CO2 laser has been used in hair transplantation procedures also. In fact, with the advantages like a bloodless field and a better cosmetic result, laser hair transplantation has replaced the conventional methods in high- tech dermatology centers all over the world. Moreover, it is possible to create recipient site slits rather than round holes with CO2 laser and this certainly gives a better cosmetic result.[9]

6. OTHER LASER SYSTEMS

i). The Copper- vapour laser

Copper vapour laser emits light at 578 nm(yellow) and 511 nm(green) in a pseudo-continuous fashion consisting of ultrashort 20 ns pulses. The stream can be shuttered into 200ms exposures and used clinically in the treatment of vascular and pigmented lesions. Bruising is less commonly seen with this laser system but the bulk of the machine and a long warm-up time are its limiting factors.[10]

ii) Q- switched Alexandrite laser

The Alexandrite laser emits red light at a wavelength of 755 nm- allowing deeper penetration in the treatment of tattoos and other pigmented lesions.

iii) Erbium: yttrium- aluminium – garnet (Er: YAG) lasers

These laser systems produce radiation with a wavelength of 2940 nm. The absorption coefficient for water at such a wavelength is quite high but the optical penetration depth is very low as compared with carbon dioxide lasers (1um vs 20 um).Any epidermal lesions can therefore be accurately ablated with this laser system and the time taken for reepithelization is also less.However the limiting factor is an increased incidence of intraoperative bleeding due to the relatively thin layer of residual thermal damage.[10]

Er: YAG lasers have been used as cutaneous resurfacing tools; in the treatment of acne scars and photoageing.

CONCLUSIONS

The introduction of new laser technology has resulted in considerable improvements in the treatment of vascular lesions, pigmented lesions and tattoos. The new generation of lasers with short pulse durations and high peak powers are capable of more selective destruction of target chromophores. More appropriate wavelength selection for different cutaneous disorders has resulted in a modest improvement in results of treatment and a substantial reduction in adverse reactions such as scarring and pigmentary disturbances.Significant advances in technology and clinical results will offer an optimistic future in this new millennium.

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BILIARY ASCARIASIS

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Ascariasis lumbricoides infests as many as 1.5 billion people around the world[1] and is particularly common is Asia, Africa and Central America. In the endemic areas 20% of the inhabitants harbor the worm. It is the most common parasite in man[2]. Poor socio-economic conditions especially inadequate facility for the sewage disposal leading to heavy contamination of the soil around the dewelling which acts as a source of infection. The disease has shown a marked reduction in the western countries owing to the ever-improving environmental sanitation.

Life Cycle :

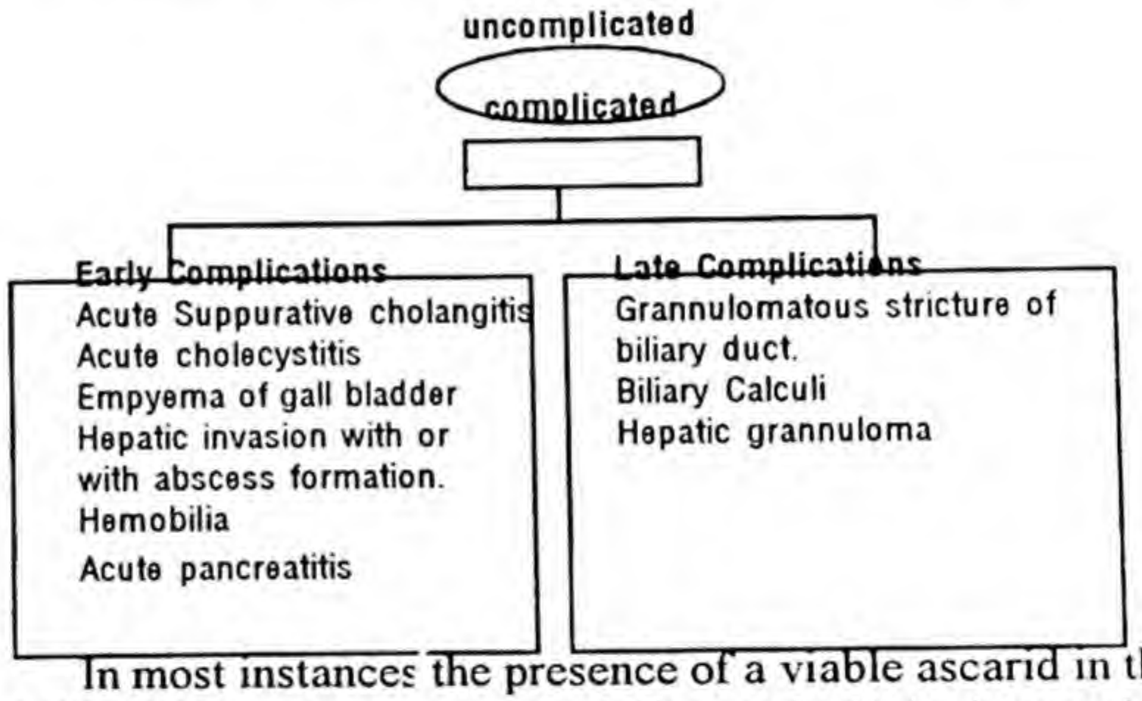
Linnaeus described the roundworm for the first time in 1758[3]. Infection in man occurs following the infestation of embryonated ova through contaminated food or dirty hands. The eggs hatch in the small gut under the influence of the digestive enzymes releasing the larvae which penetrate the gut wall to reach the small mesenteric veins and lymph channels and finally by the way of right heart to lungs. After the further development in the lungs the parasite erupts into the lung alveoli, climbs up the tracheo-bronchial tree and down the esophagus and stomach to settle in the small intestines (Jejunum) where it reaches maturity. Adult worm measures upto 15cm in length and has a life span of 1 year. The mature ova hatching in the small gut and its development into the adult worm was first described by Davine (1877); Esptain (1892) and Grass (1887-88)[3] Variation of this manner of development occurs in cases where infestation is heavy.

Biliary Ascariasis:

After intestinal obstruction and perforation, the most serious complications of ascariasis, result from migration of the worm into unusual areas within and outside the abdomen. The natural orifices of the biliary and pancreatic ducts offer a tempting pathway for ascarids on the move. Invasion of the common bile duct (CBD) by the round worm has been reported as early as 1925 by Brayne[4] and later on by a number of other observers. Muir reported gall bladder ascariasis in 1932[5].

Why the worm invades the biliary tree is not known. However, it was assumed that under the adverse circumstances such as excessive oxygen concentration there is a tenancy for the round worms to migrate from the gut and the commonest ectopic location of ascaris worm is the biliary tree[6]. This "run away movement" under adverse circumstances are a part of their biological protective mechanism[7]. Other mechanism of invasion of biliary tree is following an injury to the sphincter mechanism secondary to stone disease and surgery facilitating the duodenal content regurgitation into biliary system.

Clinically the patients condition is classfied as :-



In most instances the presence of a viable ascarid in the biliary tree causes a well delineated clinical complex characterized by upper abdominal colic, marked tenderness in the right subcostal region, worms in the stool or vomitus and a palpable gall bladder. However, jaundice is extremely rare [8-9]. Diagnosis of this condition has undergone a great revolution since the coming up of the real time ultrasonography (USG), Fig. 1,2 & endoscopic retrograde cholangiopancreatography (ERCP). On USG an 'inner tube sign' was explained by Schulman et.al.[10] and with the time it was suggested that sonography is a simple, rapid non-invasive method for diagnosis and follow up of patients with biliary ascariasis [11-12]. Other procedures which need a passing reference in detecting the hepato-biliary ascariasis include :

Percutaneous trans hepatic chonlangiography (PTC), radio isotope liver scanning, computerised axial tomography scan (CT scan), barium meal where in the ampullary cut off sign is diagnostic of biliary ascariasis, plain x-ray abdomen-(Calcified worm, pneumobilia) and intravenous cholangiography.

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BILIARY ASCARIASIS

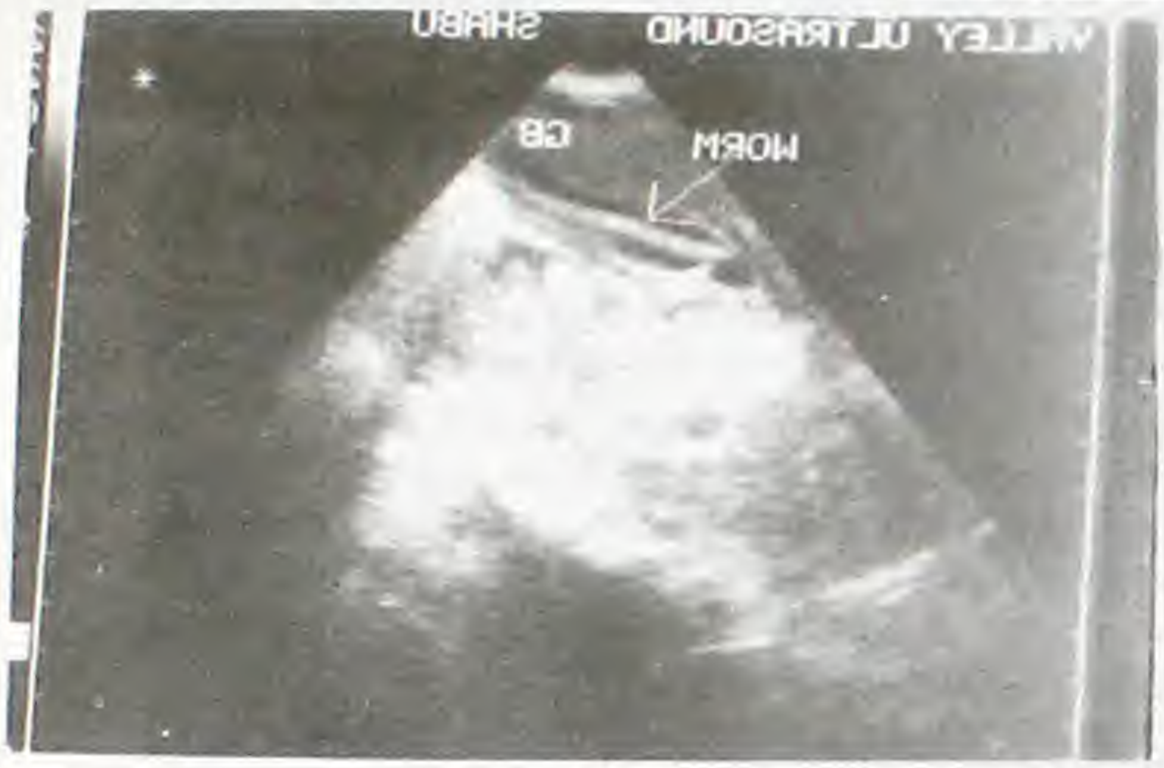

Fig.I:

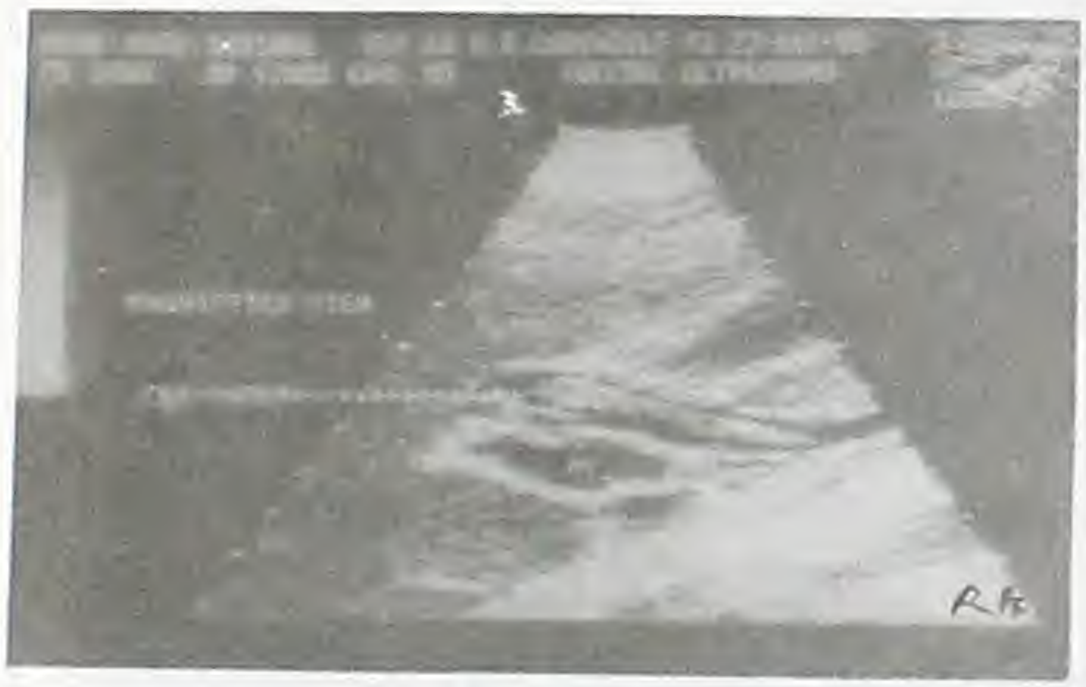

Fig. 2:

Fig.3:

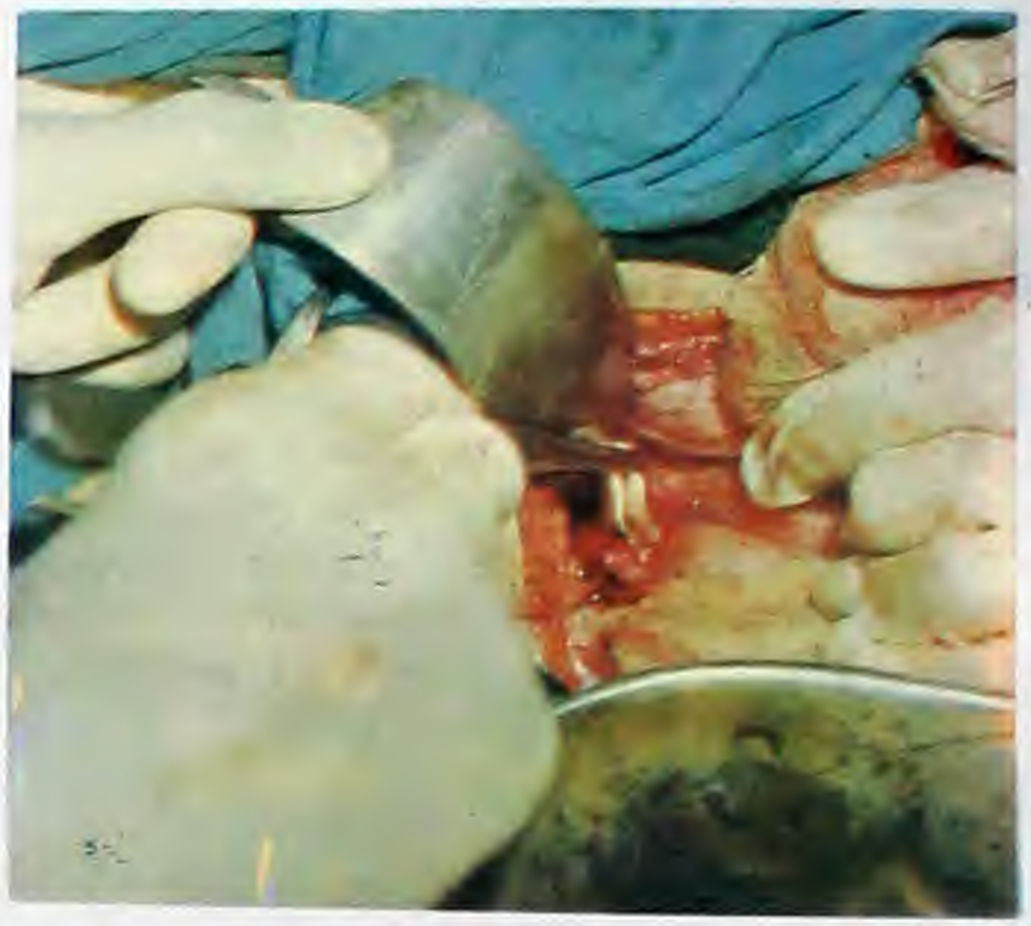

Fig.4:

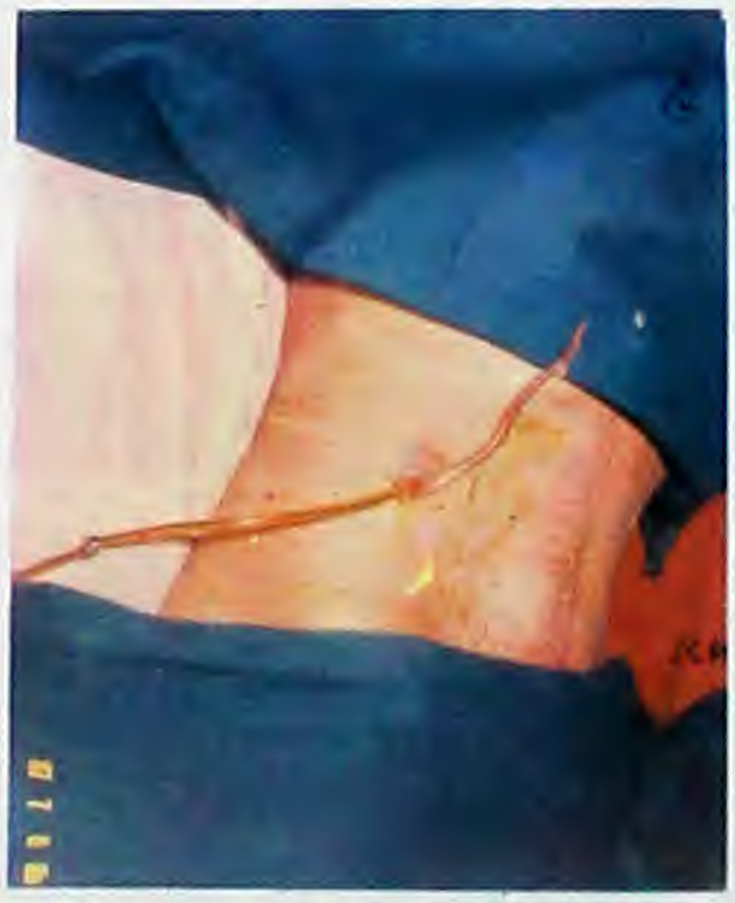

Fig.5:

LEGENDS

Fig1. Showing the ultrasonographic picture of the ascariasis worm in gall bladder.

Fig2. Showing the ultrasonographic pictures of the ascariasis in common bile duct.

Fig3. Showing per-operative picture with common bile duct full of ascariasis.

Fig 4. Showing extraction of ascariasis from common bile duct.

Fig 5. Showing worm adherent to T-tube.

Once the diagnosis is made the patient needs adequate treatment with uncomplicated cases requiring medical therapy as first approach, this usually involves ,antispasmodics, analgesics, antibiotics and once the acute attack has resolved the patient is dewormed. Follow-up is done with USG 2 to 4 weeks after antihelminthic.

Indications for surgery as defined by Chang and Han (1966) are :

i) Persistent filling defect in the biliary tree on follow-up.
ii) Persistent severe symptoms not controlled by adequate non-operative management.
iii) Clinical evidence of biliary or hepatic complications.

These principles still hold good. (Madgar *et.al.*[13]) As for the gall bladder ascariasis the treatment of choice remains cholecystectomy[14]. Recently endoscopic removal of the worm from duodenum and ampulla of vater has been recommended as an effective alternative to surgery.[15,16,17] Conventionally surgery (Fig. 3,4) involves choledochotomy, choledochoscopy assisted saline washing of CBD & IHD, cholecystectomy (if the gall bladder has worms). The evacuated biliary tree is irrigated with saline and closed over a large bore T-tube. If the intraoperative cholangiography demonstrates a biliary stricture choledochojejunostomy Roux-en-Y is recommended. One of the problems encountered in the endemic areas is the post-operative infestation of either worms over looked during surgery, worms migrated from gut i.e. re-infestation (common). This can be prevented by pre-operative anti helminthic whenever possible. And if not done pre-operatively then by an enterotomy at the time of surgery.

When identified post operatively on a T-tube cholangiogram the treatment modality involves initially expectant line of treatment with a chance that the worm goes back to the gut spontaneously. This may be assisted with T-tube flushing using 200 to 250ml of saline over 1 to 2 hrs. along with I.V. anti spasmodic, or by ERCP and extraction of worm with dormia basketing or biopsy forceps. Rarely the worm may become infected in or around the T-tube and can be removed by applying suction to the T-tube and gently with drawing it with the worm (Fig.5). If all these procedures fail than re-operation may be required.

In any case overall prognosis of biliary ascariasis is good and rarely death occurs due to septicemia associated with biliary and hepatic complications.

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ENDOSCOPIC SPHINCTEROTOMY IN THE MANAGEMENT OF THE COMMON BILE DUCT STONES: RESULTS IN 170 PATIENTS.

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Abstract: *From October 1998 to March 2001, we performed endoscopic sphincterotomy and stone extraction in 170 patients with CBD stones. Eighty-five (48.2%) patients had previous cholecystecomy. Sphincterotomy was achieved in 162 (95.3%) with overall clearance of the common bile duct in 150 (88.2%) patients. Of these 150 patients spontaneous passage of stones after ES occurred in 38 (25.3%) and instrumental extraction was performed in other 112 patients. Immediate complications occurred in 14 (8.2%) and two patients died (1.2%). Emergency laparotomy for complications was required in 3 (1.8%) patients. Twenty (11.8%) patients required surgery with failed clearance of the duct and suffered no operative mortality. Eighty-eight patients were reviewed 6-26 months (mean 18.6 ± 7.8) after sphincterotomy. Eighty-one patients remained well, free of biliary symptoms and 7 had biliary symptoms related to biliary ascariasis in 6 patients and 1 had no abnormality. We conclude that ES is an effective and relatively safe method for treatment of the common bile duct stones, both with gallbladder in situ and following cholecystectomy.*

Key words: *Common bile duct, Sphinterotomy, Stones*

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Introduction

Endoscopic sphincterotomy (ES) has become a common and widely accepted alternative to surgery in the management of the common bile duct (CBD) stones in high risk patients with an intact gallbladder and in patients with retained or recurrent calculi who has previously undergone cholecystectomy [1-3]. Most reports of ES indicate a success rate in achieving sphincterotomy of 95-98% with an overall clearance of stones from the CBD in 85-93% with a morbidity of 5-10% and a mortality of 1-2% [1-3]. In recent years, ES has been used successfully in the treatment of disorders other than CBD stones. These include pyogenic cholangitis[4], pancreatitis[5], biliary hydatidosis [6-7], and ascaris removal [8-9]. We report our experience of 170 patients who have undergone ES for clearance of CBD stones between October 1998 and May 2001.

Material and Methods

From October 1998 to May 2001, 1010 endoscopic retrograde cholangiopancreatographic procedures (ERCPs) were performed in our department. A total of 298 of these ERCPs were performed in 257 patients with CBD stones. ES was performed in 170 patients with stones < 20 mm and constituted the study group. ES was not attempted in other 87 patients for the following reasons: CBD stones larger than 20 mm in diameter (71 patients); refusal to participate (3 patients); stones located above a stricture [12]; and Polya's gastrectomy [1] Z which made ERCP impossible. Patients with stones³ 20 mm in widest diameter were referred for surgery after placement of nasobiliary drainage tube. The study group included 65 men and 105 women. Their mean age was 42.6 ± 8.2 years (range 21 to 84 years). Eighty-five (48.2%) patients had undergone previous cholecystectomy. These patients were either referred from within the hospital or from other hospitals within Kashmir. Patients were usually admitted but a few were treated as outpatients. Routine evaluation included full blood count, liver function tests, coagulation profile, upper abdominal ultrasound and other tests, if needed.

The clinical presentations included: recurrent biliary colic in 68 patients, recurrent cholangitis in 62 patients, acute pancreatitis in 21 patients and jaundice in 19 patients. ES was performed under antibiotic cover. Patients were sedated with intravenous midazolam and pentazocine. Duodenal relaxation was obtained with hyoscine butyl bromide (Buscopan). ES was performed using side-viewing duodenoscope (Olympus JF-IT10 or Pentax), pull type sphincterotome (Microvasive, Boston) and a diathermy unit (Olympus USE-2). Diagnostic ERCP was done first, and if there was a stone/s in the CBD, a sphincterotome was

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inserted into the CBD where its position was confirmed by injecting a contrast medium. Short pulses of blended cutting and coagulation currents were used to make an adequate cut. An active instrumental extraction policy was followed for stones ³ 10mm using the Dormia basket or extraction balloon. Where instrumental extraction was not successful at initial attempt or those with acute cholangitis, a nasobiliary drainage tube was inserted and stone extraction was attempted in second attempt. For patients with CBD stones ≤ 9 mm, the CBD clearance was assessed at repeat ERCP undertaken 3-4 week later on outpatient basis. A precut was performed when the CBD cannulation failed with a standard catheter.

Table1. Results of endoscopic sphincterotomy with respect to size of stones.

Size of stones	No of cases	Results of ES	
		Successful	Failure
< 10 mm	54	54 (100%)	-
10 - 15 mm	87	81 (93%)	6
16 - 20 mm	29	15 (52%)	14
Total	170	150 (88.2%)	20 (11.8%)

Results

Common duct clearance

A precut was required in 11 patients. ES was successfully achieved in 162 of 170 (95.3%) patients during the first attempt in 141 patients and in the second attempt in 21 patients. ES failed because of technical difficulty in 3 patients, impacted stone at the lower end of the CBD in 3 patients, and presence of large periampullary diverticula in 2. The biliary stones were extracted using the Dormia basket or extraction balloon after ES in 112 patients and spontaneous passage of calculi was observed at repeat ERCP in 38 patients. In 12 patients (7.4%) the CBD clearance failed because stones were too large to be extracted or passed spontaneously. The CBD was completely cleared of stones in 150 of 162 (92.6%) patients in whom ES successfully was performed (figure). Of the 150 patients with successful clearance, fragments of dead worms were also removed from the biliary ducts in 27 (20.7%) patients. All 12 patients whose bile duct could not be completely cleared after successful ES had stones ³ 15 mm in size (table 1). Overall ES was successful in removing stones from the CBD in 150 of 170 (88.2%) patients. The other 20 (11.8%) patients (8 with failed ES and 12 with residual stones after ES) were offered surgery. Nasobiliary drainage tubes were introduced in 31 patients.

Complications (table 2)

Complications occurred in 14 (8.2%) patients: bleeding in 6 (3.5%) patients, cholangitis in 5 (2.9%) patients, pancreatitis in 2 (1.2%) and basket impaction in 1 (0.6%). These complications resulted in two deaths giving a mortality of 1.2%. Emergency surgery was required in 3 (1.8%) patients. Of six patients with bleeding, transfusion was needed in one patient and surgery in none. Of five patients with cholangitis one died due to septicemic shock and multi-organ failure despite undertaking surgery 48 hours after ES. Of the 2 patients with gallstone-induced severe mecrotising pancreatitis, one recovered with conservative treatment and another died 7 days after ES. In one patient, Dormia basket was impacted with a large caught stone in the lower end of the CBD; the basket was dis-impacted with fragmentation of stone using Sochendra mechanical lithotriptor.

Table 2. Complications in 170 patients of endoscopic sphincterotomy.

Complications	No of cases	Outcome	
		Emergency surgery	Death
Bleeding	6	-	-
Cholangitis	5	3	1
Pancreatitis	2	-	1
Basket impaction	1	-	-
Total	14 (8.2%)	3 (1.8%)	2 (1.2%)

Surgery and follow-up

Eight patients with failed ES and 10 of 12 patients with residual stones after ES underwent surgery for clearance of CBD stones during the same admission and suffered no operative mortality. Two of the other patients with residual stones refused surgery. In one, unfit for surgery, endobiliary stent was introduced. This patient is well for 6 months with no clinical evidence of biliary disease. Another patient with residual stones developed cholangitis 5 months after ES and underwent surgery. Of 64 patients with intact gallbladder, elective cholecystectomy was performed in 32 patients.

A total of 88 patients were reviewed between 6-26 months (mean 18.6 ± 7.8) after ES; all but 7 were free of biliary symptoms. In 6 of these 7 patients symptoms were due to the invasion of roundworm, *Ascaris lumbricoides*, into the CBD and 1 had no abnormality. All these patients with biliary ascariasis recovered on conservative treatment with spontaneous exit of worms from the CBD into the intestines.

Discussion

The present study indicated that ES is an effective method for the treatment of choledocholithiasis. In our series, sphincterotomy was achieved in 95.3% with overall clearance of stones from the CBD in 88.2%. Other

investigators reported a success rate in achieving sphincterotomy in 95-98% with an overall clearance of CBD in 85-98% patients [1-3].

The immediate complications of ES (bleeding, cholangitis, pancreatitis and retroperitoneal perforation) occured in 7-10% of patients with mortality between 1 and 2%. Majority of these patients in most large series have been referred for endoscopic treatment by surgeons. Therefore, these rates of morbidity and mortality must be interpreted with this background. Long-term complications (mainly papillary stenosis and/or new stone formation) have been reported upto 10% (10-11). Most of the immediate and long-term complications can be managed effectively by endoscopy . In our study, complications occurred in 8.2% of our patients, emergency surgery was required in 2.4% and deaths occurred in 1.2%. Both of our patients who died after ES were critically ill because of underlying disease; one because of severe gallstone-induced severe nacrotizing pancreatitis and another because of suppurative cholangitis. Impacted Dormia basket in the CBD with caught stone was successfully disimpacted using Sochendra lithotriptor without resort to surgery.

Nasobiliary drainage was inserted in patients with cholangitis and/or in those whose stones were larger than 10 mm that could not be extracted at the first attempt. In these patients biliary drainage prevented stone impaction and further development of cholangitis. Of 150 patients with successful CBD clearance, stones passed spontaneously in one-fourth of patients and instrumental extraction was needed in another three-fourths. Stones smaller than 10 mm in diameter usually slip into the duodenum after adequate sphincterotomy. Residual stones after adequate sphincterotomy occurred in 12 patients and in all of them extraction failed, as stones were larger than [illegible] mm in diameter. In large series, 10-18% stones defy [illegible]val using standard Dormia baskets or extraction [illegible] catheters, frequently because the stone is large in size (³ 15 mm in diameter), impacted or located above a narrowed CBD segment, or presence of juxtaampullary diverticulum. Recently, a number of nonsurgical treatment options are available for extraction of these difficult stones which includes, mechanical lithotripsy [12], electrohydraulic lithotripsy [13], laser lithotripsy [14] and extracorporeal shock wave lithotripsy [15]. All these techniques involve stone fragmentation prior to removal. Although stone size is an important factor, the large CBD stones of the brown and pigment variety are often soft and muddy and can be easily crushed with a Dormia basket and extracted. We extracted soft stones upto 20 mm in diameter. Therefore, stone size alone is not the only factor of failure; equally important is the shape and consistency of the stone, diameter and shape of the exit channel and the nature of the stricture of the CBD below the stone.

Fig. A. Retrograde cholangiogram shows common bile duct packed with multiple stones.

Fig. B. Cholangiogram after extraction of all stones

The CBD stones constitute the commonest indication for ES, accounting for greater than 80% of patients [1-3]. In 20.7% of our patients who underwent successful ES, stones coexisting with dead, fragmented roundworms were extracted. This form of biliary disease producing soft pigment stones is common in Kashmir [8-9]. ES has become an established mode of treatment for CBD stones in the elderly and high risk patients with previous cholecystectomies [1-3]. ES carries relatively less mortality (0.5-2%) [1-3] compared to surgery [16]. Furthermore, ES eliminates the hazards of general anesthesia, laparotomy, choledocholithotomy, and prolonged immbolization. Use of ES in young and surgically fit chloecystomized patients with CBD stones is controversial but ES is favored because it is simple, less expensive and safe. Likewise, the use of ES in patients with gallbladder in situ remains controversial[17]. However, ES has been shown to be a safe procedure in elderly, high risk patients and in otherwise fit patients with an added risk for surgery such as cholangitis[4]. Results of long-term follow-up of ES in patients with gallbladder in situ have shown that incidence of

cholecystitis increased twice if gallbladder harbor stones; however, intact gallbladder without stones was not an additional factor after ES.

The recurrent biliary symptoms in majority of our patients were due to biliary ascariasis. In endemic areas of ascariasis, patients undergoing ES are prone to suffer from recurrent invasions of biliary tree by ascarides because widen papilla facilitates the passage of ascarides from the intestines into the biliary tree. The regular and an effective 2-monthly course of antehelmintic can significantly reduce this complication[9].

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PROSPECTIVE RANDOMIZED COMPARATIVE STUDY OF EARLY SURGICAL EXCISION AND CONSERVATIVE TREATMENT FOR DEEP BURNS OF HAND

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Abstract: *A prospective randomized comparative study was carried in 50 patients (72 hands) with deep dorsal hand burns, over a period of 3 years. Twenty five patients (35 hands) were treated conservatively by local antimicrobial cream (silver sulfadiazine) and late grafting when needed, while 25 patients (37 hands) were treated by early surgical excision and skin grafting at a mean of sixth post burn day (range 3 to 12 days). Physiotherapy was the same for both the groups. Patients were followed for a period of 12 to 24 months.*

We have observed that early surgical excision and immediate skin grafting shorten healing time, morbidity and lessens hospital stay. The number of anatomic deformities and the total number of reconstructive procedures were much reduced in the primarily excised group. Long term functional and cosmetic results in the excision group were also superior to those obtained in the conservatively managed group. These results encourage the routine use of primary excision and immediate for all deep dorsal burns of hand in patients with burn size of less than 40% of total body surface area.

Key words: *Burns, Excision, Hand, Treatment.*

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Introduction

The hand is a very important part of the body and has a vital functional importance. As the hand is used in manipulatory and exploratory functions, it is exposed to all sorts of hazards, thus is one of the most commonly burned areas of the body.[1] Although the skin of the hand constitutes only 5 percent of total body surface area,[2] severe burns of dorsum of hand if not managed properly and promptly, may result in permanent disability and crippling deformity. Keeping in view the functional importance of hand, there is no margin for error in treatment. The surgical management of acute deep burns of hands ranges from old traditional or conservative therapy to early surgical excision. Early surgical excision ranges from direct fascial excision to sequential (tangential) excision. Both treatment modalities offer theoretical benefits, but little data exists which would document the superiority of either technique in preserving the hand function. Burns are very common in our part of world, due to use of kangri and other forms of fire in chilly cold winter, with the hand being one of the most commonly involved parts. This has prompted us to achieve a true comparison and to point out the important consequential results which differentiate the two controversial modalities of treatment for burns of hands.

Material & Methods

The study was a randomized prospective study of 50 patients (72 hands) with deep dorsal hand burns admitted at Sher-i-Kashmir Institute of Medical Sciences, Srinagar, from January 1995 to January 1998. Patients with extensive burns, inhalational injuries, superficial dorsal hand burns, palmar burns, obvious charring or gangrene of digits were excluded from the study. The patients were randomly allocated to two groups according to the card pulling system. Twenty five patients (35 hands) with deep second and third degree dorsal hand burns were treated with topical silver sulfadiazine cream without excision and were allowed to heal spontaneously and when necessary were closed with auto skin graft after eschar had completely separated and a healthy bed of granulations formed. Twenty five patients (37 hands) were subjected to excision within 12 days after injury followed by immediate autografting. In majority of patients[19] the surgical excision was carried out within the first post burn week, however, surgery was delayed in 6 patients until second post burn week, because of delayed referral in 5 patients and extensive burn (42% of total body surface area) in one patient where survival was the primary objective.

Immediate systemic management of burned patient was same in both groups and only after the patients were stabilized, was the management of burned hand initiated. The initial management during immediate post burn period in either group consisted mainly of control and prevention of infection by daily cleansing and topical silver

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sulfadiazine dressing followed by immobilization of the hand and fingers in functional position using volar splints (Fig.1).

For the patients undergoing surgical excision, two surgical techniques were employed. Patients with unquestionable and uniform full thickness burns of hands were subjected to direct facial excision using a sharp scalpel and patients with mxied deep dermal and full thickness burns, underwent tangential (sequential) excision using a free had Watson skin grafting knife followed by immediate split thickness autoskin grafting of the excised area. Postoperatively hand was immobilized in functional position using volar splints. The grafted hands in either group were first inspected on third post operative day when gentle physical therapy was begun. The hand was then rewrapped and the process repeated. After the tenth postgrafting day, a progressively vigorous programme of active and passive exercises was begun. When all the grafts had stabilized, the patients hands were fitted with compression garments (Fig. 2). Patients were followed up regularly, the period of follow up varied from 12 to 24 months in either groups.

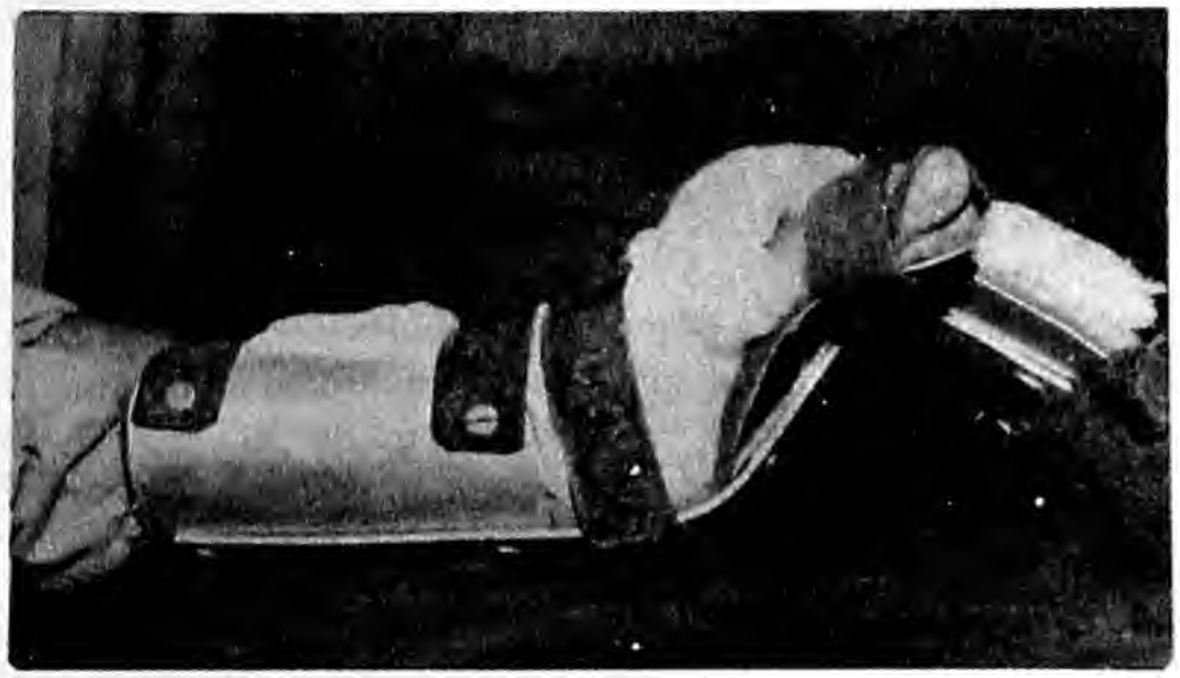

Fig-I: Hand Splinted in functional position

The evaluation included recording for each group the number of hand deformities developed and the total number of reconstructive procedures performed for their correction. The long term functional and cosmetic results of hands were carefully analyzed. The functional results were assessed by active and passive joint movements, key pinch and mass grip and the patients ability to use hand in day to day tasks. The assessment of cosmetic appearance was subjective, however, an attempt was made to quantitate the outcome by analyzing burn wound contour surface characteristics, presence of blisters and hypo or hyperpigmentation.

The outcome was evaluated using following criteria:

1. Excellent	Normal or near normal function and normal or near normal appearance.
2. Good	Near normal function with compromised appearance.
3. Poor	Compromised function with unacceptable appearance.

Chi Square and Fisher's Exact test were employed for comparing proportions. Continuous variables were tested by Students 't' test. The results as excellent, good, and poor were secored as 3, 2, and 1 respectively and the mean scores were compared using tests for continuous variables.

Results

There was no significant difference between the two groups with respect to the distribution of age, sex, percent total body surface area burns, the period of follow up and for the depth of burns. Only two patients, one in each group had burn size of more than 30% total body surface area (TBSA). Most of the patients (80%) in the excision group were discharged from hospital within 3 weeks when 92% of the patients in the conservative group were still in the hospital at that time which is statistically highly significant (P<.001). Thirty three (94%) hands in the conservative group had late complications in contrast to only 16 (43%) in the excision group (P<.001). Two hands in the conservative group and one hand in the excision group had insignificant hypertrophic scars which did not interfere with function and needed no reconsruction. Similarly one hand in the conservative group and one in excision group who had insignificant thumb contracture and flexion contracture respectively were not subjected to reconstruction till last follow up.

Thirty hands (80%) in the conservative group required secondary reconstruction in contrast to only 14 hands (38%) in the excision group which was statistically highly significant (P<.001). It was also observed that the total number of reconstructive procedures were much higher in the conservative group reaching statistical significance at 0.1% level. The functional and cosmetic results were significantly better in the excision group (P<.001) as shown in Table I.

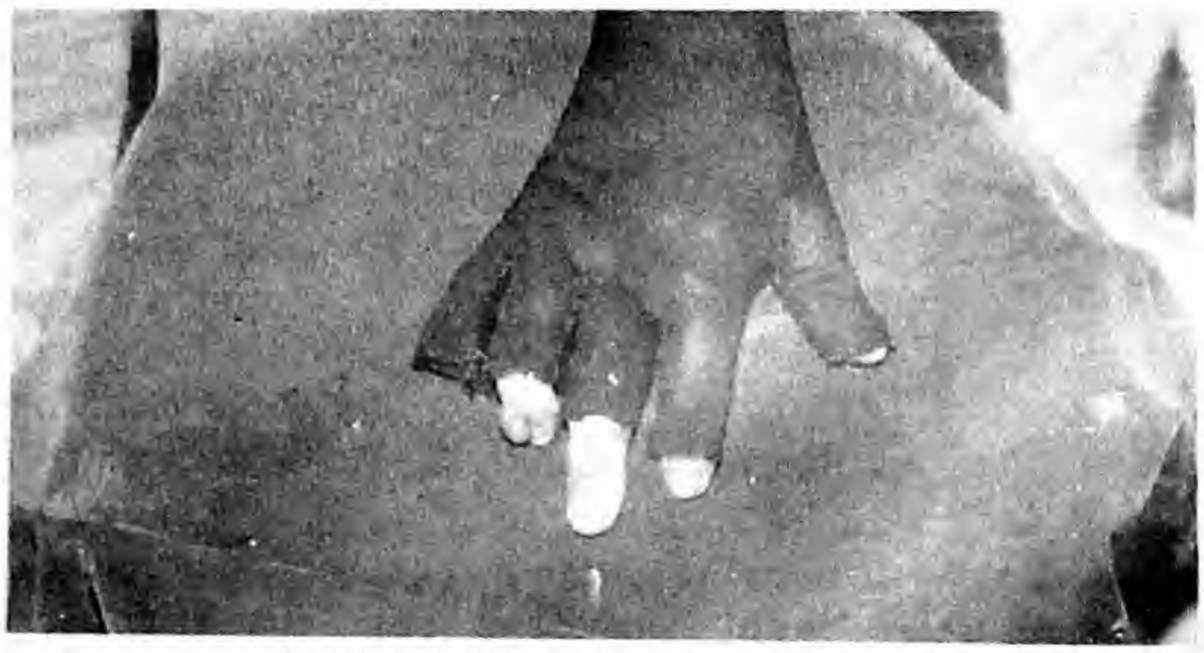

Fig-II: Hand in compression glove.

Discussion

The management of deep dorsal burns of hands has been a controversial issue. A number of treatment modalities have been tried for the burned hand, some advocating topical antimicrobial agents alone, and/or multiple debridements with late grafting [3-5]. While others propose early surgical excision.[6-8]

In a burned patient, the main stay of work out is survival followed by reduction in complication rate and then for maintenance of function of the affected part. Patients with more than 40% total body surface area burn, who are excised and grafted do not share the same functional gains as those with less than 40% burn (total body surface area).[9] Patients with extensive burns, have a priority of survival first, who are invariably complicated by hypovolumia, shock, infection and multiorgan failure and need multiple transfusions. In such patients excision of hands has a low priority. Studies of such patients in India involving primary excision and prompt skin grafting have been disheartening.[10] Hospital stay is one of the important parameters which need to be considered for any type of treatment, because of hospital cost, limited bed strength, hospital acquired infections, morbidity and loss of working hours. Early surgical excision and grafting shorten hospital stay in patients who do not have otherwise a large total body surface burns.[10,11] Statistically significant difference was found for hospital stay between the conservative and early surgical group in various comparative studies[12-14] which goes in accordance with our study. Burke et al[15] in their comparative study of 200 patients reported that, it takes longer time to achieve wound closure in patients treated conservatively.

Table I: comparison of Functional and Cosmetic Results

Results	Conservative group (N=35)	Excision grup (N=37)
Excellent	2	16
Good	23	15
Poor	10	6
Score (Mean±SD)	1.77±0.55	2.27±0.73

One of the commonest complications of burn wound healing is hypertrophic scaring, however wounds that are primarily closed show less hypertropic scaring as compared to wounds which are allowed to heal spontaneously. A reduction in hypertrophic scarring in "in determinant" depth burns treated by early srugery was shown by Engrav et al.[13] Although most of these patients had burns affecting areas other than the hand. Inspite of vigorous exercises. use of pressure garments, and splinting programme, scar complications (boutonniere deformity, finger contractures, web space and thumb contractures) still occur after deep dorsal hand burns,[16] especially in children because of their difficulty in understanding the severity of problem and complying with treatment programme of splinting and exercises. However, the number of such deformities and need for their reconstruction have been reported to be much less by early surgical excision and immediate grafting,[14,17,18] the results being consistent with our study.

Bondoc et al[17] in their series of 60 children reported that 29 (97%) patients in the conservative group required secondary reconstructive procedures for the correction of their hand deformities however, the figure was only 16 (53%) patients in the surgical group. The number of times a hand/patient needs reconstruction is an important consideration as it means, readmission, reexposure to anaesthesia and further surgical trauma. Burke et al 1976[18] reviewed 152 patients with hand burns. Half were treated conservatively and half by early surgical excision. They reported that the latter approach reduced the need of secondary reconstructive procedures. Mahler et al 1987[14] also reported a statistically significant reduction in secondary surgery in patients with hand burns undergoing early surgery. However, our results are contradictory to those of Edstrom et al 1979[16] becuase these authors concluded that early surgery for deep partial thickness hand burns conferred no advantage over conservative treatment in terms of number of secondary reconstructive procedures. This may be because of the fact that these authors had excluded full thickness hand burns from their study.

Functional outcome is the most important concern in the management of a burned hand. Early surgical excision and immediate grafting gives better functional and cosmetic results than traditional conservative treatment.[14,17,18] There have been many reports of functional assessment of hand burns. They vary widely in the timing of the assessment and the parameters studied. Levine et al 1979[8] showed that in a group of 50 patients with 71 burned hands who underwent early surgery, only 50% of deep dermal burns achieved good hand function. However, this assessment was made at only 6 weeks from the date of injury. Flexion, extension, abduction, contracture and ability to perform every day tasks were all taken into account.

Pegg et al 1984[19] reported moral hand function in 80% of deep hand burns treated by early surgery and included full thickness burns. Functional assessment was made by the measurement of grip strength but the timing of the assessment was not given. The requirement of secondary reconstructive procedures should provide a further outcome parameter in these patients.

Levin et al[9] graded functional results as good, fair and poor and reported good results in 64% and fair in 15% patients (treated by tangential excision and grafting) and added that 4 of every 5 patients (79%) were having a functional hand (good plus fair). Mahler and Hirshowitz[20] reported good functional results in 62 (90%) hands in his

series of 69 (59 patients) treated by tangential excision.

In our series in the surgically excised group 23 hands (62%) had excellent fucntion and 11 (30%) had good function when the figure was 5 (14%), 25 (71%) respectively for the conservatively treated grouup. However, when the achievement of a functional hand (excellent plus good) were compared by Chi Square Tet, the significant difference between two groups vanished, which would satisfy Goodwin et al.[21]

Cosmetic appearance of dorsum of hand needs special consideration especially in young females in the management of deep dorsal burns of hands. Our results were comparable to those of Burke and associates.[18] Engrave et al[13] in his series reported that both forms of therapy had similar results with regard to presence of blisters and skin contour. However, the excised group had increase in surface irregularity, largely due to the use of meshed skin grafts.

It is therefore concluded that early surgical excision and grafting shortens healing time, morbidity and lessens hospital stay enabling the affected individual to return quickly to work and normal routine life, prevents long and unfavourable delay in healing, scar formation and its incapacitating sequellae.

The number of anatomic deformities and the total number of reconstructive procedures for their correction were much reduced in the primarily excised group.

Long term functional and cosmetic results in the excision group were superior to those obtained in the conservatively managed group.

These results encourage the routine use of primary excision and immediate skin grafting for all deep burns of dorsum of hand in patients with burn size of less than 40% of total body surface area. These patients should be referred immediately to the specialized units for proper management in order to avoid complications.

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APPENDICULAR PERFORATION DUE TO ASCARIASIS IN CHILDREN OF KASHMIR

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ABSTRACT: *In Kashmir the incidence of ascariasis is very high. Mainly the children from low socio-economic group who are literate and whose standard of living is poor are mostly affected. Dangerous complications may arise from the wanderlust of the worms and their tendency to explore orifices, ducts and cavities. Appendicular perforation though very rare is a grave problem. We are reporting 11 cases of appendicular perforation out of our series of 441 cases which were admitted either as intestinal obstruction due to ascariasis or acute worm colic, over a period of 10 years, with effect from January 1988 in the age group of 3–14 years. Patients which showed rising pulse rate in absence of any mass, toxaemia out of proportion to severity of obstruction or fixity of mass for more than 48 hours with increased abdominal distension were taken for surgical intervention (Dayalan criteria).*

121 patients taken for surgery as per above criteria in our series. 11cases which were having either appendicular perforation alone or associated with other bowel lesions due to ascariasis were our operative findings, as the diagnosis of appendicular perforation due to ascariasis, preoperatively is very difficult are reported. All the cases reported here were thoroughly studied. Clinical history, preoperative and operative findings and results of various operative procedures and complications are reviewed. Earliest surgical intervention is stressed to decrease the morbidity or moriality. Mass deworming of the children is suggested.

Key Words: *Ascaris lumbricoides Gangrene, Resection, Appendix, Perforation, Sutures.*

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INTRODUCTION

Surgical ascariasis is still a formidable problem in some tropical countries like India.[1] In the valley of Kashmir the incidence of ascariasis was observed as 85.1% of total helminthic and protozoal infected cases[3]. Mainly the children from low socio-economic group who are illiterate and whose standard of living and personal hygiene are poor are affected.[3,4,5] Parasites that infest the alimentary tract of man, the round worm appears to be the most versatile in its effects.[1, 6] large number of patients who attend our out patient departments for the treatment of other problems are found to be suffering from ascariasis after advising 3 consecutive stool examinations[5,6]

Group of patients who report with severe abdominal colic or as intestinal obstruction are very alarming and challengeable for the surgeon. Ascarids may reach the abnormal situations and cause acute complications. They have been seen in pancreatic duct, bile duct and Eustachian tube [3,5] because of their migratory tendency to explore the orifices and ducts may lead to variety of other dangerous complications and may attract considerable notice because of severe prognosis.[1,3,7]

They may cause small bowel volvulus, intussusception,[8] bile duct obstruction,[3,9] acute cholecystitis,[3,5,10] hepatic abscess,[8] pseudopancreatic cyst,[3] acute pancreatitis,[3,10] and acute appendicitis.[7] Meckel's diverticulitis or its perforation due to round worms or passage of worms through patent vitello-intestinal duct into umbilicus are rare.[7,12,13]

Wandering ascarids have been seen to cause even localized abscess on abdominal wall by burrowing into it and resultant necrosis with perforation of adjacent viscera, like genitourinary tract have been reported.[6,14,15] granulomatous masses may form around the eggs released from the female worms which have escaped into the peritoneum and mimic tuberculous peritonitis.[8]

According to Dayalon[16] the various criteria for surgical intervention in patients admitted as acute worm colic or intestinal obstruction due to ascariasis are as follows:

- Persistence of mass at same site or fixity of mass for more than 36 hours.
- Persistence of abdominal pain and tender mass.
- Rising pulse rate in absence of any mass.
- Toxaemia out of proportion to the severity of obstruction.

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There is no specific method for diagnosing the surgical complications of ascariasis and the mode for treatment is still controversial more so when the conservative treatment should be stopped and the child be subjected to laparotomy.[3,4,9]

We are presenting a series of 11 cases who were having appendicular perforation due to ascariasis either alone or associated with other bowel lesions.

MATERIAL AND METHODS

11 cases of appendicular perforation are presented , out of which 6 were females and 5 were males in the age group of 3–14 years, out of our series of 441 cases of acute worm colic/acute intestinal obstruction due to worms were studied over a period of 10 years with effect from January 1988. This study includes only the appendicular perforation due to ascariasis or associated with other bowel lesions due to ascariasis. Diagnosis was confirmed by accurate history, clinical examination, stool examination, abdominal radiography, ultrasonography and other routine investigations. Surgical intervention was done as per Dayalon criteria.[3]

Table 1: Persisting complaints in children with ascaris bowel obstruction.

Signs and Symptoms	*No. of Patients*
Abdominal pain	11
Distension of abdomen	11
Vomiting	6
Constipation	5
Fever	7
Passing of worms per rectum	6
Passing of worms in vomitus	4
Palpable mass of worms	6
Tenderness	8
Rebound tenderness	9
Bleeding per rectum	2

Rising of pulse rate in absence of any mass, toxaemia out of proportion to the severity of obstruction, persistence of mass at the same site or fixity of mass for more than 36 hours were taken into consideration for earliest surgical intervention. Preoperative diagnosis of appendicular perforation due to ascariasis is very difficult, and cases reported here are based on operative findings of the patients who were taken for surgery.

All the patients who were admitted, nothing was given orally. Nasogastric decompression was done along with intravenous fluids and metronidazole, and patients were given proper antibiotic coverage. Surgical intervention was done as per Dayalon criteria. Appendicular perforation due to wandering ascarids were thoroughly studied.

Out of 11 patients who were having appedicular perforation, 4 cases were also having impacted worms in the ileocaecal region. Massaging of worms into colon was done along with appendectomy, besides enterotomy in two patients. The buried stump of appendectomy was covered with omentum patch. 2 cases in our series were having gangrenous changes in the ileum, with appendicular perforation. The gangrenous bowel was resected and primary end to end anastomosis was done using nonabsorbable sutures in two layers besides appendectomy. Simple appendectomy was performed in 2 cases and stump was covered with omentum patch. Appendectomy and Meckel's diverticulectomy was done in one patient who presented us with perforation of both.

Average hospitalization was 7–10 days and all the cases were followed in the OPD.

2 patients had a severe malnutrition and were in poor general condition. Minor wound infection occurred in 3 cases.

There was a anastomotic leak in 1 patient which was managed by slow suction with povidine irrigation and proper parenteral nutrition for a period of 1½ months, but patient died of toxaemia.

DISCUSSION

Ascariasis is more common in the poor underdeveloped countries of Asia, Africa and tropical regions due to poor sanitation and unhygienic conditions as prime factors for conducive to the growth of ascarids. It is estimated that 25% of the world population is infected with ascarids[15]. In Kashmir the incidence of ascariasis was observed as 85.1% of total helminthic and protozoal infected cases.[2]

Dangerous complications may arise from the wandering lust of the worms and their tendency to explore orifices, ducts and cavities.[13,17] Appendicular and Meckel's diverticular perforation due to ascariasis are rare.[1,15]

11 cases in our series were having appendicular perforation due to ascariasis. Louw reported only 2 cases with symptoms of acute appendicitis due to obstruction of the lumen of appendix in his series of 731 cases in children.[9] in our series of 441, case no. 3 was having Meckel's diverticular perforation in addition to appendicular perforation also due to ascariasis which is very rare.[1]

There is no definite criteria for diagnosing the appendicular perforation due to ascariasis preoperatively. In our series of cases of appendicular perforation due to worms all were admitted as cases of intestinal obstruction due to ascariasis and may give vague idea for diagnosing a case of appendicular perforation due to worms.

Table 2: Operative findings

Findings	*No. of Patients*
Simple appendicular perforation	4
Meckel's diverticular perforation	1
Appendicular perforation with impact of worms at ileocaecal region	4
Appendicular perforation with gangrene of bowel (Ileum)	2

Table 3: Surgical procedures performed

Procedures	*No. of Patients*
Appendectomy with burying of stump	2
Appendectomy with massaging of worms into colon	4
Appendectomy with enterotomy	2
Appendectomy and Meckel's diverticulectomy	1
Appendectomy and segmental resection with primary anastomosis	2

The ascariasis infestation is usually asymptomatic but the principal complications occur because of obstructions and perforation of intestinal wall.[4] In our series of 441 cases of worm infestation 11 cases showed signs of localized peritonitis associated with obstruction which revealed appendicular perforation due to ascariasis at laparotomy.

Louw[17] reported 2 cases of appendicular perforation due to worm obstruction of lumen of appendix and resultant perforation at the tip of appendix with escape of ascaris into the peritoneal cavity. Both the cases in his series died within 36 hours of hospitalization. In our series of 11 cases perforation of appendicular lumen at tip was noticed in 4 cases and at base of appendix was noticed in 7 cases and in all cases worms were found free in the peritoneal cavity, only 1 case of appendicular perforation was found having associated patent vitello-intestinal duct which is very unusual presentation.

Case no. 3 was having associated Meckel's diverticular perforation with free worms in the peritoneal cavity which is very rare entity.

Dickson and Cole(1964) reported cases of ileal perforation with *Ascaris lumbricoides* in the peritoneal cavity in cases of typhoid fever.[18]

Ihekwaba(1979) presented 3 cases of ileal perforation caused by round worm, direct pressure by bolus of worms, ulceration and necrosis would seem to be the most obvious mechanism of perforation of bowel.[19]

All our cases responded well as surgical intervention was done immediately, only 1 patient died of septicaemia due to anastomotic leak postoperatively 1½ month after surgery. As compared to our study Pinus J(1982) reported appendicitis due to ascariasis in 8% of cases with 2 deaths in his series of 454 cases.

Navarrane(1949) reported that *Ascaris lumbricoides* had caused postoperative intestinal anastomosis disruption between 3rd and 6th day of operation resulting in peritonitis.[20] There is no reported case of any series having appendicular and Meckel's diverticular perforation in a same patient as was in our series in case no. 3. Also in our series besides appendicular perforation presence of patent vitello-intestinal duct is not reported.

About 20% cases of Meckel's diverticulum become inflamed giving rise to symptomology almost identical to that of acute appendicitis. Important precipitating factors for Meckel's diverticulitis are the accumulation in the pouch of coarse intestinal residue, foreign body or enterolith.[12]However very rarely an ascaris which is ascending or descending the ileum, could enter the orifice of Meckel's diverticulum.[13]

Villigar(1929) reported a case in which 64 ascarids had filled Meckel's diverticulum. Paul(1972) reported a case of Meckel's diverticulitis with round worms in the peritoneal cavity though neither orifice of exit nor the leakage of intestinal contents in the peritoneal cavity could be seen[8] as compared to our case no. 3 which was having perforated Meckel's diverticulum with free worms in the peritoneal cavity. In our series of 11 cases of appendicular perforation of ascaris, the possibility of intestinal perforation by *Ascaris lumbricoides*, though unlikely but are produced by acute inflammatory process obstruction and damage of the bowel wall. This damaged wall may then be perforated by vigorous effort of these worms.[7] As can be well judged, a preoperative diagnosis of *Ascaris lumbricoides* causing appendicular perforation could not be made but perforated appendix was diagnosed on the basis of physical signs supported by the history of having been given purgative or vermifuge as was seen in our series wisp like radiolucent lines in plain X-ray of the abdomen as observed earlier may help in diagnosing a case of appendicular perforation due to ascariasis.[4]

Sinha(1974) suggested a probable diagnosis of association of *Ascaris lumbricoides*.[4]

There is general agreement of managing these cases by doing appendectomy burying the stump and fixing omentum patch over it. Meckel's diverticulum is resected and primary end to end anastomosis is done in 2 layers.[4]

CONCLUSION

We conclude our study that:

Dangerous complications may arise from the wandering lust of ascarids. Mass deworming of the children is suggested. If there is any evidence of deterioration of patient as per Dayalon criteria, patient should be taken for surgical intervention immediately, to reduce the mortality.

Proper clinical history – present and past, supported by X-ray abdomen, ultrasonography, may help in getting the diagnosis at the earliest.

If possible worms should be massaged into the colon,

and if not possible enterotomy should be done to remove the bolus of ascariasis, besides appendectomy. Appendicular stump should be buried with omentum patch fixed on it.

If associated with gangrenous gut secondary to worm obstruction resection with primary anastomosis should be performed.

Purgation during acute worm colic should be avoided.

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PATTERN OF HIRSCHSPRUNG'S DISEASE IN KASHMIR VALLEY - A 3 YEAR STUDY.

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Abstract: *A 3 year study revealed that Hirschsprung's disease is the commonest cause of constipation in the paediatric age group in Kashmir Valley. Out of a total of 38 cases with constipation, Hirschsprung's disease accounted for 68.42% with a ratio of 1.16:1 in favour of males. it was found to be most prevalent in the 1-3 year age group. Short segment disease was found to be more common.*

Key Words: Hirschsprung's disease, constipation.

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Introduction

Hirschsprung's disease is a congenital disorder of bowel motility that usually presents in the neonatal stage with inability to pass meconium within first 48 hours of birth. It is characterized by absence of ganglion cells usually in the rectosigmoid region (short segment variety). The transition zone between ganglionic and aganglionic intestine may be funnel like because of the presence of a few ganglia. Aganglionosis typically extends to the rectosigmoid region in 80% of cases (short segment type) however, in some cases it may extend to whole colon (total colonic aganglionosis) or may be limited to very small segment of rectum (ultra-short segment).[1]

The basic embryologic defect in Hirschsprung's disease is the failure of craniocaudal migration of neural crest cells in the distal part of the colon.[2] These neural crest cells fail to migrate because of abnormal distribution of fibronectin and laminin in the extracellular spaces in patients with aganglionic bowel wall.[3] The intestine contains intrinsic nervous system and the neurotransmitter responsible for is Nitric oxide,[4] which is formed by the enzyme Nitric oxide synthase. In Hirschsprung's disease there is loss of the enzyme, with the result that the aganglionic segment fails to relax and acts as a functional obstruction of the colon.

Material and Methods

This study was conducted in the Departments of Paediatric Surgery and Pathology, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar. A total of 38 cases of constipation were studied over a period of 3 years from November 1997 to October 2000. Of these 26 patients met the criteria for Hirschsprung's disease i.e., (1) clinical radiological features consistent with Hirschsprung's disease (2) histopathology.

The data abstracted included:

1. Medical record number
2. Age of presentation of symptoms
3. Clinical presentation
4. Sex
5. Birth order
6. Type of Hirschsprung's disease.

Observations

We recorded in the tabulated form following observations that were made during our 3 year study of the patients who met the criteria of Hirschsprung's disease.

Table I: DISTRIBUTION OF CASES OF HIRSCHSPRUNG'S DISEASE ACCORDING TO AGE (n=26)

AGE	NO.OF CASES	PERCENTAGE
0-1 month	6	23.07
1 month - 1 year	2	7.69
1 year - 3 years	9	34.61
3 years - 8 years	7	26.92
8 years - 9 years	2	7.69

Age of the presentation of symptoms ranged from immediately after birth to 9 years. The mean age was 35.28 months. Majority of cases 9(34.61%) presented between 1-3 years of age.

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Table II: SHOWING SIBLING HISTORY OF HIRSCHSPRUNG'S DISEASE

Total No. of patients	26
Sibling history found in	2
Percentage	7.69

Sibling history was found in 7.69 percent of our patients.

Table III: SEX-WISE DATA (n=26)

SEX OF PATIENTS	NO.OF PATIENTS
Male	14
Female	12

In our series we had 14 males and 12 females. Thus male female ratio of Hirschsprung's disease was 1.16:1 in favour of males.

Table IV: DISTRIBUTION OF CASES ACCORDING TO PLACE OF RESIDENCE (n=26)

PLACE OF RESIDENCE	NO.OF PATIENTS	PERCENTAGE
Rural	21	80.76
Urban	5	19.24

Eighty percent of our patients were from rural areas. This is because most of our population lives in rural areas.

Table V: PRESENTING SYMPTOMS OF THE CASES (n=26)

SYMPTOMS	NEONATES (n=6)	INFANTS & CHILDREN (n=20)
Inability to pass meconium within 48 hours of birth	6(100%)	History not available
Chronic constipation	x	19(95%)
Abdominal distension	5(83.33%)	14(70%)
Vomiting	4(66.66%)	x
Bleeding PR	2(33.34%)	x

More than one symptom was present in majority of cases.

Table VI: DISTRIBUTION OF CASES WITH REGARDS TO HIRSCHSPRUNG'S ASSOCIATED ENTEROCOLITIS (HAEC) n=26

	NO.(%)	MORTALITY NO. (%)
Patients with enterocolitis	5(19.23)	3(11.53)
Patients without enterocolitis	21(80.77)	Nil

Enterocolitis was a major cause of morbidity and mortality in our series.

Table VII: ANALYSIS OF SHORT SEGMENT DISEASE VERSUS TOTAL COLONIC AGANGLIONOSIS

VARIETY OF HIRSCHSPRUNG'S DISEASE (n=26)	NO. OF CASES	PERCENTAGE
Short segment disease	20	76.94
Ultrashort segment disease	3	11.53
Total colonic aganglionosis (TCA)	3	11.53

Short segment disease was the commonest variety of Hirschsprung's disease found in our series. TCA was found only in 3(11.53%) of our cases.

Discussion

We here report the demographic pattern of Hirschsprung's disease. In our study the age of the patients was between 0-9 years. Maximum cases 9(34.61%) belonged to the age group of 1-3 years. Fourteen (53.48%) of our patients were males and 12(46.16%) were females. Thus male to female ratio was 1.16:1. Reding R et al[5] in his experience of 20 years in Hirschsprung's disease found a male female ratio of 2.5:1. In our series we observed a sibling history of this disease in two patients (7.69%). Ryan et al[6] noted in his series of 179 cases a sibling history of Hirschsprung's disease in 13 cases (7.3%). Reding R et al[5] observed a sibling history of this disease in 7 percent of his 59 patients.

In our study we had 2 groups of patients - 6 neonates (23.07%) and 20 infants and children (76.93%). Clinical presentation in neonatal Hirschsprung's disease included abdominal distension in 5 patients (83.33%), vomiting in 4 cases (66.66%), inability to pass meconium within first 48 hours of life in all the 6 cases (100%). The clinical features in older infants and children (n=20) included constipation in 19 cases (95%) and abdominal distension in 14 cases (70%). Same clinical profile has been reported by Jung[7] who observed abdominal distension in 90% of his cases and vomiting in 67% in neonatal Hirschsprung's disease. The incidence of constipation and abdominal distension in older infants and children was 68.7% and 64% respectively. We observed that 30.76% of patients were first born. Ryan et al[6] also reported incidence of Hirschsprung's disease in 28% of white children.

In our study we observed Hirschsprung's disease associated enterocolitis (HDAEC) in 5 of our cases (19.23%). All the five were neonates. Such patients came with fever, tense abdomen and bleeding per rectum. Out of 5 patients, 3 expired (11.53%) and 2 were saved by conservative management. Jung[7] reported in his series 24.30% incidence of enterocolitis in neonatal

Hirschsprung's disease. Thus our observation regarding the incidence of Hirschsprung's associated enterocolitis tallies with what has been reported in literature.

In our series we found that 3(11.5%) of total 26 patients had total colonic aganglionosis and 20 cases (76.92%) had short segment disease involving rectum and rectosigmoid and 3 patients (11.5%) had ultrashort segment disease. Thus short segment variety affecting the recto-sigmoid is the commonest form of this disease. Reding et al[5] also observed in his series, short segment variety in 75%, total colonic aganglionosis in 15% and ultrashort segment in 5%. His 5 percent patients had Hirschsprung's diseases of unknown length because of their death without autopsy.

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ILIZAROV TECHNIQUE OF RADIAL LENGTHENING FOR LOWER RADIAL EPIPHYSEAL GROWTH ARREST

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Abstract: *Ilizarov technique is an effective and comparatively safe procedure for lengthening of short radius secondary to lower radial epiphyseal growth arrest or Madelung deformity. A series of six cases is presented and goal of treatment has been achieved in all cases. Both deformity correction and lengthening has been achieved.*

Key words: *Short Radius - Ilizarov technique - Bone lengthening.*

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Introduction

Isolated radial shortening is most often due to trauma or growth arrest of distal radial epiphysis. Malunion or nonunion can also present with isolated radial shortening[1]. Madelung deformity is also an inherited cause of radial shortening with deformity. If premature epiphyseal closure occurs at an early age, severe shortening will cause marked cosmetic and functional deficit. Shortening of less than 2 cms can present with ulnar impingement, diminished grip strength, prominence of ulnar head and possible loss of pronation and supination[2]. When shortening is 3 cms or more, the presentation is a club hand deformity with loss of dorsiflexion, palmar flexion and severe prominence of distal ulna[1,3,4].

There are only few reported cases of forearm lengthening in literature[4,5]. Distal ulnar resections or repeated ulnar shortening may restore alignment at the expense of forearm shortening and weak grip. Wagner's technique of lengthening including bone grafting and plating has most often been used but did not gain much popularity because of high complication rate[3,5,6].

Ilizarov introduced a method of lengthening limbs based on the biology of the bone and soft tissue regeneration under conditions of tension stress. Although the spectrum of potential complications are unchanged bone healing problems are less common and goals of treatment are usually achieved[7]. We present a series of radial lengthening for radio-ulnar discrepancy secondary to lower radial epiphyseal growth disturbance.

Material and Methods

We performed radial lengthening by the Ilizarov technique on six patients with radial shortening secondary to lower radial epiphyseal growth disturbance. There were two female and four male patients with mean age of 16 years. Four patients had radial shortening secondary to traumatic distal radial epiphyseal growth arrest and two patients had radial shortening secondary to Madelung deformity. All patients complained of aesthetic deformity and functional difficulties interfering with their daily life and school activities with occasional pain.

Operative Technique:

In all six patients a two ring construct was made preoperatively Under general anaesthesia and under control of torniquete, the Ilizarov frame was mounted on the forearm and each ring stabilised with two wires at each end. At the distal end two wires were inserted into radius within 5-10 mm of the wrist joint. Oblique wire was inserted from volo-radial to dorso-ulnar aspect lateral to volar artery and vertical wire antero-posteriorly medial to palmaoris longus. At the proximal end the wires were inserted at the level of mid-forearm, both oblique and vertical wires being placed parallel to distal wires. Corticotomy of distal radius was done at metaphyseal level through 1-2 cm radius incision with 5 mm osteotome. Physical therapy was started on Ist post-operative day, initially passive followed by active range of motion as pain decreased. Distraction was started on 7th day at the rate of 0.25 mm four times a day radiograph was done at one week post distraction to check the separation of fragments. On alternate weeks the clinical and radiographic review was done and at about 4 weeks bone formation was visible in the distraction gap. In two cases radius was over distracted by 0.5 mm to reduce the prominence of ulnar head and to compensate for residual growth of lower end of ulna and also to improve motion The Ilizarov apparatus was removed after clinical and radiographic confirmation of union and long arm cast was applied for four more weeks prophylactively.

Results

Lengthening of radius was achieved in all patients.

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Table-1:

Diagnosis	Age	Sex	Side	Radial cms	Lengthening %	Treatment time (months)	Lengthening index months/cm	Complications	Follow up months.
1. Distal radial epiphyseal growth arrest	16	m	Left	3.4	18	4	1.2	*PTI-Gr 1	36
2. -do-	18	F	Right	1.5	7	2½	1.7		24
3. -do-	17	M	Left	1.4	6	2½	1.8		30
4. -do-	17	M	Right	3.5	19	4	1.1	PTI-G1	12
5. Madelung deformity	12	F	Left	1.4	6	4	2.8		18
6. Madelung deformity	16	M	Right	2	10	5	2.5	PTI-Gr1	24

* *PTI Pin Tract Infection*

There was mean lengthening of 2.2 cms; range 1.4 cms to 3.5 cms. These represented a 6% to 19% increase in initial radial length. The total treatment time was an average of 3.7 months; ranging from 2½ to 5 months. The mean lengthening index (the number of months per cm of lengthening) was 1.8 month/cm. The lengthening index was more for Madelung deformity otherwise for simple lengthening it was only 0.9 month/cm (Table 1). The follow up ranged from 12 months to 36 months (average 24 months). Further subjective evaluation was done for functional, cosmetic and and psychological improvement. Cosmetic and psychological improvement was achieved in all patients. There was marked improvement in range of motion of wrist. Two patients had mild restriction of dorsiflexion of wrist without any functional impairement. Deformity was corrected in all cases except in one case of Madelung deformity where subluxation of lower end of ulna was persistent as only minimal correction of volar tilt of distal articular surface of radius was achieved due to premature consolidation of the regenerate.

Discussion

Limb lengthening procedures have most often been applied to lower limbs. The discrepancy in the length between two upper extremities does not produce significant functional deficit. It is because of this and for fear of functional loss that lengthening of the forearm has rarely been performed for shortening of forearm. There are only few reported cases of forearm lengthening in the literature which have occasionally been performed for discrepancy in length between the radius and ulna[4,5]. In view of high complication rate Wagner's technique of lengthening did not gain much popularity[3,6,8].

Ilizarov technique has opened new doors for the treatment of such limb length discrepancies. It relies on bone and soft tissue regenerate without the need of bone grafting. Prokopovich 1980 was the first to reporte using Ilizarov technique in 3 cases of shortened forearm bones that were successfully lengthened. Villa et al 1990[4] is credited for the first English language article on forearm lengthening by Ilizarov technique. He lengthened 13 forearms in 12 patients and goal of treatment was achieved in all patients despite 81% complication rate. Functional and cosmetic improvement was noticed in 92% of his patients. 3.5 cms (22%) was maximum radial regenerate achieved. 5 cases of radial club hand deformity treated had improved grasp post-operatively with increased flexion and mild loss of extension. A series of lengthening and deformity correction of upper limbs including two cases each of distal radial growth arrest and Madelung's deformity and achieved good cosmetic and functional end results[9,10].

In the forearm there are specific considerations which are not problematic in lower limb lengthening. The forearm bones are small in diameter, thus large lengthenings tend to narrow the diameter of the regenerate because of the push of the surrounding muscles. This leads to bubble gum effect (narrowing of the centre as one stretches the bubble gum). When this occurs, one must narrow the gap and then lengthen it again. This can be done by compressing the distraction gap by 1-2 mm/day for 5-10 days and then resuming lengthening at a reduced rate of 0.5 mm/day (Villa et al 1990). Lengthening rate should also be reduced or temporarily stopped when radiolucent interval is exceeding 5 mm during distraction, development of significant pain and contractures that cannot be managed by splinting or therapy.

Flexion contractures of the elbow, wrist or fingers should be prevented by vigorous physiotherapy, extension splints during rest and night. In some cases wrist is fixed by transmetacarpal pin which should be removed at the end of distraction.

Neurovascular injury is a potential complication with transfixation pins and can be minimised by having thorough knowledge of cross sectional anatomy of forearm at each level of fixation, safe wire insertion technique, exposure of bone where the chances of damage to important neurovascular bundle is high as in the proximal radius. Pin associated nerve palsy can be minimised by using a nerve stimulation test, to test each pin where the risk of nerve damage exists. If a stimulus results, the pin can be re-directed or moved to another location. Distraction related nerve injury is rare and is usually preceded by sensory prodrome. Suspection of hyperaesthesia can prevent progression of these injuries If distraction related nerve

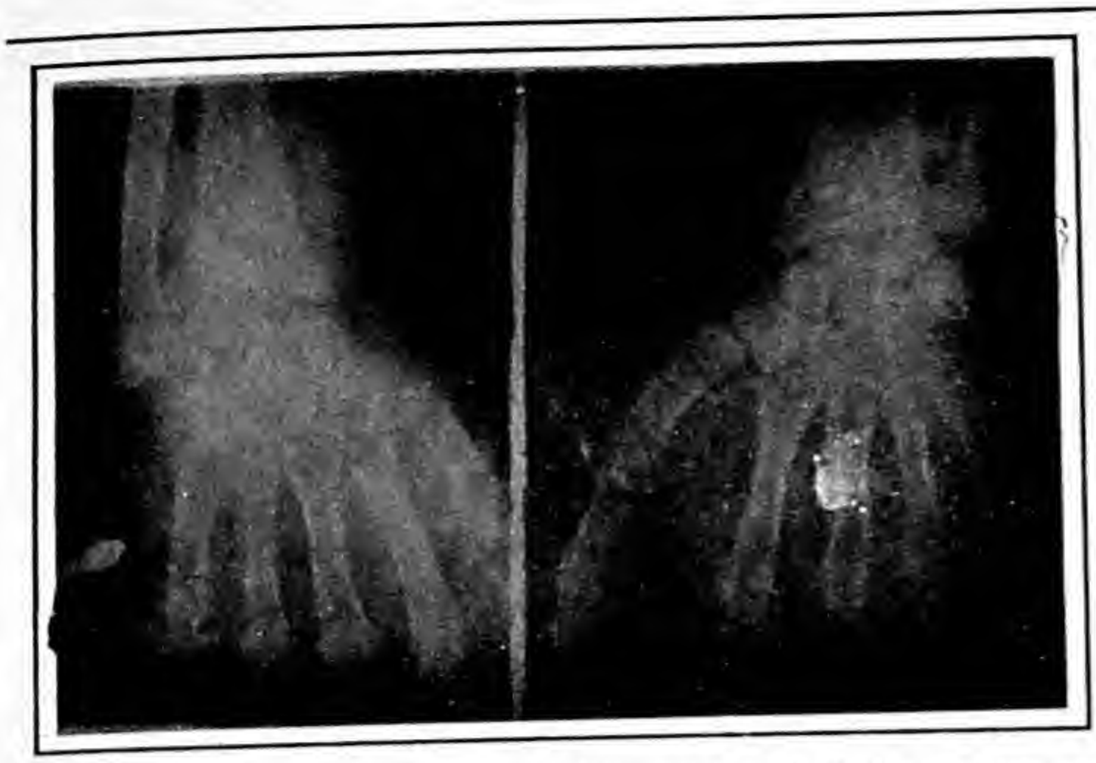

Fig. 1 Photographs of wrists showing radial shortening and subluxation of inferior radio-ulnar joint on leftside.

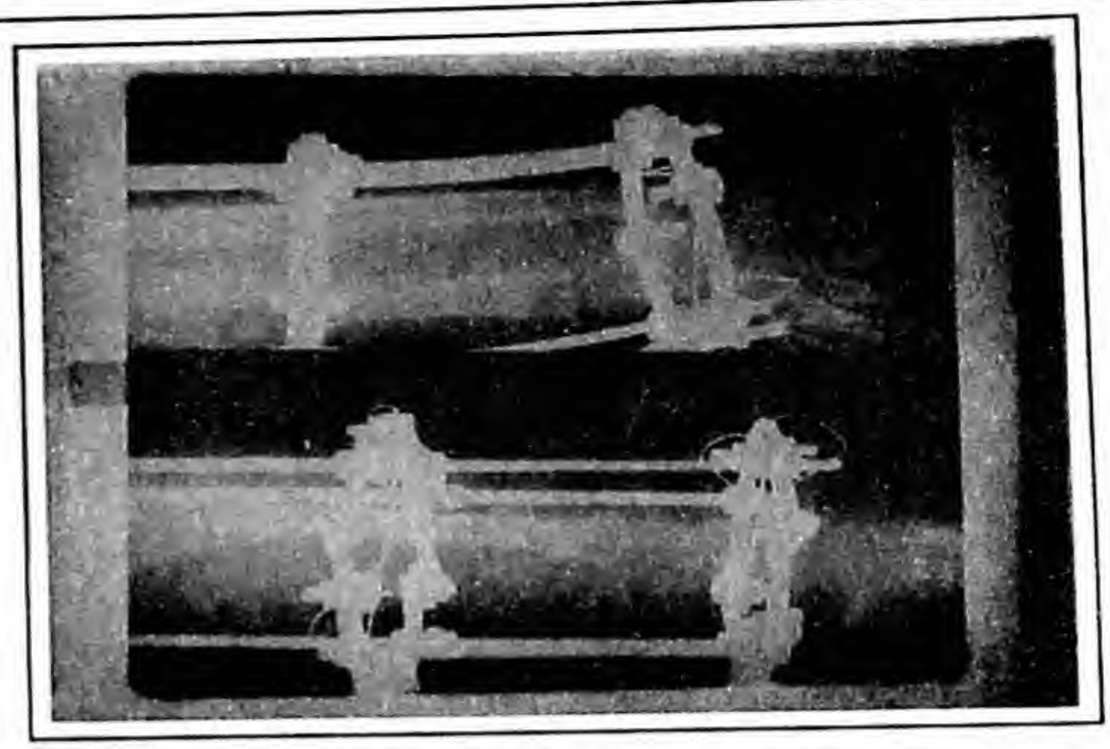

Fig. 2 . AP and Lateral Radiographs showing good regenerate

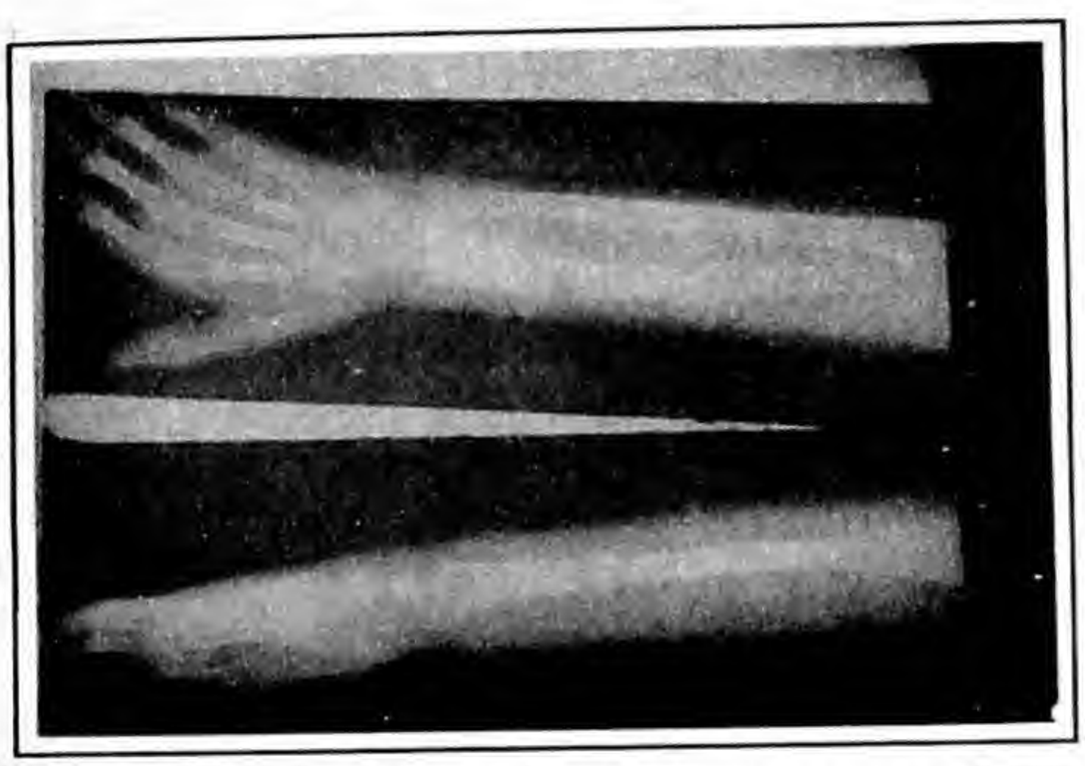

Fig. 3 AP and lateral radiographs showing consolidation of regenerate and corrtection of radio-ulnar discrepancy

Fig. 4 Photograph showing normal dorsiflexion of wrist on leftside.

injury is identified, the bone is allowed to consolidate. Lengthening can be completed through a new corticotomy at a new location.

Thus Ilizarov technique if properly performed is an excellent device for achieving radial length andcorrecting the deformity as well. The smaller diameter pins of Ilizarov are advantageous over large diameter threaded one half pin fixator. The half pin fixator have large pin inproportion to the diameter of the bone and may lead to large holes in the bone with loosening and possible fracture through the pin site. In Madelung deformity, the radial lengthening with reaxation of distal articular surface of radius may prove a worth while procedure.

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SENSATION OF A LUMP IN THROAT AND OBSESSIVE COMPUSIVE DISORDER – IS THERE A LINK?

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Abstract: Sensation of vague pain, discomfort or a lump in throat (globus hystericus) is a very common presenting symptoms especially among the patients attending ENT, gastroentrology and chest medicine services. In this study 3 patients presenting with these complaints without any organic cause and not responding to the treatment had a detailed psychiatric evaluation after ENT consultation. Psychiatric workup revealed a diagnosis of moderate to severe obsessive compulsive disorder and responded well to psychiatric treatment. Need for psychiatric evaluation of patients presenting with vague throat complaints and its possible link with obsessive compulsive spectrum disorder is discussed here.

Key words: *Throat, Lump, Globus, obsession, compulsion, link.*

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Introduction:

Obsessive compulsive disorder (OCD) has been an area of scientific scrutiny since the time of Esquirol who in 1838 in his Psychiatric text book described OCD patient as being "chained to actions that neither his reason or emotions have originated, that his conscience rejects and his will can not suppress."[1] The Diagnostic Statistical Manual of 4th Edition of the American Psychiatric Association DSM IV defines obsessive compulsive disorder as presence of obsessions of compulsions that are source of significant distress or impairment and person recognizes that obsession and compulsion are excessive or unreasonable.[2] Obsessions are recurrent, persistent thoughts, images or impulses that are experienced as intrusive and inappropriate. Compulsions are repetitive behaviours (e.g. counting, repeating) that the person feels driven or mental acts to perform in response to an obsession or accordingly to rigid rules. Globus, the Latin word for hump indicates a sensation of having a lump in the throat.[3] Alternative terms used are globus hystericus, globus pharyngeus, globus syndrome. Historically globus was described by Hippocrates as a symptom related to the wondering uterus putting pressure on neck.

Case Report I

A 28 year old married graduate female was referred for psychiatric evaluation from Department of ENT. This female had developed non-specific throat symptoms particularly feeling of lump in throat from last few years for which she was variously treated by GP's, gastroentrologists and ENT surgeons but to no avail. Psychiatric evaluation of the patient revealed young well dressed female looking of stated age seemingly in distress because of the disorder. Further examination revealed that thought content was full of various obsessions commonest among them included contamination fears, fear of losing things, fear might harm others, fear will be responsible for something else terrible happening and main theme of the corresponding compulsions was excessive ritualized hand washing, need to repeat routine activities and mental rituals (checking, counting) etc. Patient was rated with Y-BOCS scale[4] (Yale Brown – Obsessive Compulsive Scale) – the most widely used rating scale for OCD.

Total Y-BOCS Score = 33 (Extreme illness)

Patient was put on clomipramine 75 mg and after several weeks of combination of pharmacotherapy with behavioural therapy employing exposure and prevention of ritualistic responses the patient had considerably improved.

Case Report II

A 39 year old married male reported working as Lab. Technician to Psychiatric OPD after extensive investigations for his chronic non specific throat symptoms revealed nothing and his distress continued. Ten years back he first time went to an ENT surgeon with sensation of feeling ball in throat which he variously described as pebble, tennis ball, etc. During these ten years he underwent upper GI endoscopy, Indirect Laryngoscopy, Direct Laryngoscopy, Thyroid function profile besides other routine investigations.

Psychiatric evaluation revealed long history of recurrent, intrusive thoughts about cleanliness particularly while he was handling laboratory material. He recognized the irrational nature of these obsessive concerns. Administration of Y-BOCS check list revealed many aggressive obsessions like fear might harm others, fear will act on unwanted impulses – sexual obsessions like forbidden on perverse sexual thoughts. Compulsions were particularly distressing concerning excessive hand washing, checking rechecking, etc. Y-BOCS administration revealed

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a score of 30 i.e. severe disorder. 8 Weeks after 100 mg of cloimipramine therapy majority of the symptoms had ameliorated.

Case Report III

A 25 year old married female whose first pregnancy aborted and her father died suddenly few months ago came to ENT, OPD with non-specific throat symptoms. ENT work up was completely normal and was referred to psychiatry. Initial psychiatric evaluation revealed mild depressive features. But Y-BOCS checklist administration revealed a 'chronic washer' with thought content formed of predominant contamination obsession. Y-BOCS score was 24 i.e. moderate OCD. Patient was put on Fluoxetine 40 mg and is recovering fast.

Discussion

Non organic sensation of lump in throat 'globus' is a common viseral conversion disorder, symptom ranking as fourth after vomiting aphionia and painful extremities. Besides conversion disorder it is not so uncommon a complaint in other subtypes of somatoform disorders like somatization disorder, sontoforn pain disorder and hypochondriasis. Psychoanalysts related Globus sensation to the close association of feeding and crying in infancy.[5] Certain other studies have related gobus to neurosis,[6] depression[7] or panic attacks.[8] Although neither of the two diagnostic systems currently followed all over the world i.e. DSM IV and ICD IO have any diagnostic entity with features of globus associated with obsessive compulsive symptoms but the authors feel that the conditions of a substantial percentage of patients presenting as 'globus hystericus' could be better conceptualized as a part of obsessive compulsive spectrum disorder. Some of these patients on detailed evaluation may even qualify for being labelled, according to either of the above mentioned diagnostic systems, as a full fledged case of obsessive compulsive disorder.

Obsessive compulsive disorder presents as 'infinitely personalized variations on a small number of morbid themes – aggression, harm avoidance, contamination distasteful or excessive sexual ideation, religious concerns, collecting, need for symmetry or order, need to know, and fear of illness. The patients inner experience is disturbed by persistent, intrusive fear, dread of being guilty, pathological doubt, repugnant images or urges and or a need to carry actions to completeness or perfection.[9,10,11]. OCD impaires patients quality of life.[12]

Dysfunction in a neuronal loop running from orbital frontal cortex to cingulate gyrus, striatum globus pallidus thalmus and back to Frontal cortex has been implicated in pathogenesis.[13]

Another hypothesis which has wide acceptance is abnormality in serotonergic neurotransmission.[14] Twin studies and family studies suggest genetic predisposition.[15] The recent findings that an antigen which is a genetic marker for Rheumatic fever susceptibility is also a marked for susceptibility to an autoimmune form of childhood onset OCD.[16]

OCD as an Autoummune disorder triggered by a Group AB Haemolytic streptococus (GABHS) infection has been established in children but whether autoimmune factors play role in adult onset OCD remains to be elucidated.[17]

Non specific throat symptoms and its association with OCD in our view is being discussed first time, with the hope that further studies will be stimulated which will result in better understanding and treatment of these patients.

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PHEOCHROMOCYTOMA PRESENTING AS MYOCARDIAL INFARCTION:

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Abstract: *Pheochromocytoma is a rare tumor arising from chromaffin tissue in adrenal medulla or in other paraganglia of the sympathetic nervous system[1]. It is commonly seen in young to mid adult life with slight female predominance. Pheochromocytoma occurs in .1% of the hypertensive population[2], which if untreated or mistreated can be fatal. We present a case managed as migraine for 3 years and subsequently found to have Pheochromocytoma when she presented with Myocardial Infarction.*

Key words: *hypertension, migraine, myocardial inarction, Pheochromocytoma*

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Case Report

A 37 year old white female was in good health till 1998 when she started developing headaches and palpitations. At that time she was diagnosed as migraine and treated with propranolol. Over the period of 2 years she continued to suffer from episodes of headache, sweating and palpitations. She presented to Emergency Room in August 2000 with severe headache. She was found to be hypertensive on admission and ECG showed ST segment inversion in inferolateral leads. Cardiac enzymes were normal but Troponin I was elevated. Patient was managed with Verapamil with some improvement in symptoms. Echocardiogram showed left ventricular hypertrophy and Coronary Angiogram was normal. She was discharged on antihypertensive medications.

After 3 months she presented to Emergency Room with dull substernal chest pain radiating to neck and middle of back. On examination her heart rate was 120/min, BP 180/90mmhg and rest of the physical examination was unremarkable. The EKG revealed T wave inversion in leads II, III, AVF, V4, V5 and V6. Laboratory values revealed Troponin T 1.2 ng/ml (<0.10), CK 261IU/L (24-170), MB fraction 29.5 ng/ml (0.0-9.0) and Relative index 11.3% (0-4). Chest radiography showed diffuse alveolar infiltrates and Echocardiogram showed diffuse hypokinesis of left ventricle. She was diagnosed as having Myocardial Infarction and admitted to Coronary Care Unit.

She became drowsy, cold and clammy with mottled skin after receiving intravenous Metoprolol with paradoxical increase in blood pressure. At this point Pheocharomocytoma was suspected and random urinary Catecholamine level was measured which revealed Epinephrine level of 19435 ug/g createnine (2-16), Norepinephrine 9166 ug/g creatinine and Total Catecholamine 2919 ug/g creatinien. Utrasound of abdomen revealed a soft tissue mass measuring 5.3x4.5x4.8 cm in size along the superior aspect of right kidney. Phenoxybenzamine was started with gradually increasing doses and labetolol was subsequently added. Her blood pressure decreased to normal and her symptoms improved. Repeat Echocardiogram after few days showed improvement of left ventricular function to normal level. She subsequently underwent resection of the tumor and the biopsy showed histologic features of Pheochromocytoma.

Discussion

Pheochromocytoma induced Myocardial Infarction is rare. Catecholamines produced by Pheochromocytomas have direct injurious effect on myocardium[3,4,5]. In addition they lead to myocardial damage by increasing metabolism of myocardium and causing coronary vasospasm. Myocarditis and Cardiomyopathy may also be associated with Pheochromocytoma. If Cardiomyopathy is identified early it can be remarkably reversible with pharmacological blockade and later removal of tumor. Cardiac dysfunction on admission improved dramatically in our patient after treatment with α and β blocker. Irreversible Dilated Cardiomyopathy may result from prolonged exposure to circulating Catecholamines. The histologic picture of myofibrillar degeneration with interstitial infiltration by mononucleocytes with secondary fibrosis and calcification is seen in such cases[6]. A similar Catecholamine induced Cardiomyopathy has been described in patients with

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prolonged sympathetic overàctivity in Tetanus. Hypertrophic Cardiomyopathy may result from Norepinephrine induced hypertension. Pheochromocytoma is a great mimic and presents in huge variety of ways. It should be considered in the differential diagnosis of a young patient presenting with Myocardial Infarction.

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HEREDITARY SPHEROCYTOSIS PRESENTING WITH MIGRATORY POLY ARTHRITIS REPORT OF TWO CASES IN A FAMILY AND REVIEW OF LITERATURE

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Abstract: *Hereditary spherocytosis is usually an autosomal dominant disorder. The red blood cells, instead of being concave, are spherical with decreased ratio of surface area to volume. Besides the usual clincial features of anemia, splenomegally and jaundice, there are some other associated manifestations as well. We report the disorder in two members of a family, with migratory polyarthritis as an unusual feature in one of the siblings.*

Key words: *Anemia, erythocytes, jaundice, spherocytosis.*

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Introduction

Hereditary spherocytosis is usually an autosomal dominent disorder of variable experession, occuring in both sexes with an approximate incidence of 1:1000 to 1:4500[1]: The disorder occurs due to a wide variety of metabolic and structural aberrations of cytoskeleton of erythrocytes[2]. Anemia, jaundice and splenomegaly are the usual clinical features. In addition, other features like gallstone formation, leg ulcers and various other manifestations are charactristics of the disorder. We report the disorder in two siblings of a family, amongst whom the younger one developed migratory polyarthritis which is an unusual association of the disorder, not reported in previous literature.

Case Report

Two siblings, the product of a non-consanguinous marriage, second and third in birth order were studied to have the disorder. There was no historical evidence of the disease in the family pedigree from maternal or paternal side.

Case 1: A 23 year old female, presented with two year history of yellowish discoloration of eyes, off and on pain right hypochondrium, and feeling of fullness in abdomen. There was no such history of illness in any other person in the locality nor was there any history of blood transfusions or percutaneous needle pricks, or drug intake. Examination revealed the patient anaemic with mild icterus, and splenomegaly. Rest of the examination was normal. Amongst the investigations her hemoglobin was 7.8g/dl, with spherical red blood cells in the peripheral blood smear. Leucocytes and platelets were normal. The red cell-osmotic fragility after 24 hours of incubation was increased. MCV was normal and MCHC increased to 38%. Reticulocyte count was increased in 18% liver function tests revealed serum bilirubin 4.8 mg/dl. Ultrasonography of the abdomen revealed cholelithiasis and splenomegaly. Skeletal survey did not reveal any abnormality. Other possible causes of spherocytosis like cirrhosis, glucose-6-phosphate dehydrogenase (G6PD) deficiency, were excluded.

Case 2: A 19 year old boy 3rd in birth oder, younger brother of Case 1, was admitted for evaluation of recurrent jaundice and splenomegally, and migratory polyarthritis. Examination revealed patient of average built, anaemic, with splenomegaly, and arthritis, of major joints (left knee and ankle iniitially), which involved small joints as well during hospital stay, and responded to non-steriodal anti-inflammatory agents.

Investigations, revealed patients anemic with hemoglobin of 8.5g/dl, and spherical red cells on peripheral blood film. The white blood cells and platelets were normal. The erythrocytes again showed increased osmotic fragility and MCHC (37%) and reticulocyte count was elevated to 12%. Liver fucntion tests showed bilirbun 3.5mg/dl, predominently unconjugated. There was no other biochemical or endocrinological abnormality; and septic screen and profiles of collagen vascular disease and rheumatic fever proved negative.

On the basis of clinical and laboratory features, the diagnosis of hereditary spherocytosis was made in these cases. Both patients were subjected to splenectomy and cholecystectomy with uneventful postoperative period. On followup, patients had improved symptomatically, and there was marked improvement of anaemia as well. We monthly, monitor their clincial and hamatological parameters.

Bone marrow aspiration revealed erythroid hyperplasia, other cell lines were unaffected. Ultrasonography again revealed cholelithiasis and splenomegaly skeletal survey did not reveal any abnormality.

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Discussion

Hereditary spherocytosis is a common disorder, usually autosomal dominant and equally common in males and females[1,2,3]. Although identification of the disorder in multiple generations of affected families is the rule, nearly one quarter of newly diagnosed patients have parents who are clinically and hematologically normal[2], as is true with our cases. The absence of hematologic abnormalities in family members suggests either autosomal recessive inheritance, or less commonly, spontaneous mutations[1,2]. The diagnosis is made by family history and typical clinical and laboratory findings[1,2]. A variety of possible metabolic and structural defects have been found of pathogenic significance for hereditary spherocytosis, including spectrin deficiency and defective spectrin protein binding leading to defective membrane skeleton of erythrocytes; altered membrane properties due to loss of surface area, altered membrane lipids, and calcium; defective protein phosphorylation and increased sodium permeability, glycolysis and ATP turn-over, or decreased phosphoenolpyruvate transport[1,2,3,4]. Anemia, jaundice and splenomegally are the major clinical manifestation of hereditary spherocytosis[1,3,4].

Beyond these features, there are also some associated manifestations as well. There may be episodes of bone marrow failure referred to as aplastic crises most commonly precipitated by infection. Aplastic crises of a more gradual onset may result from folic acid deficiency possibly due to increase in the rate of deoxyribonucleic acid synthesis, which is most pronounced during pregnancy. Anemia may also occur due to accelerated rate of hemolysis called hemolytic crisis; which usually occurs in response to infection[2,5,6,7,8]. Other associated conditions include chronic leg ulcers[1,2,3,4], chronic dermatoses[2], growth and skeletal disorders, hemosiderosis, multiple endocrine disorders, primary carcinoma of the gallbladder, and tower-skull appearance "turmschadel" and prominent maxillae with thalasemic facies have also been reported[1,2,3,4]. In our second case, the development of migratory polyarthritis is a very unusual feature. The cause of which remained unknown despite extensive investigations. This manifestation of arthritis has not been reported in the earlier literature.

Regarding therapy, splenectomy almost always corrects the anemia, although the erythrocyte defect and its consequent morphology persists[1,4]. However a mild decrease in red cell survival has been seen in few patients undergoing splenectomy, resulting in mild anemia or no anemia at all, with fluctuating degrees of jaundice[4]. The operative mortality of splenectomy approaches that of anesthesia alone, however risk of acquiring infection increases with an incidence of 0.5% in the older age group[4,10]. Most hematologists agree that hereditary spherocytosis after spleenectomy is consistent with a normal life expectancy. Our patients who are presently doing well, are under our regular followup.

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PERFORATION OF LIVER - A RARE COMPLICATION OF HEPATOBILIARY ASCARIASIS

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Abstract: *Although biliary ascariasis is common, the hepatic variety is rare. Perforation of the hepatic parenchyma by ascaris is even rarer. Only two cases have been reported so far. We add one more case of hepatic perforation by ascaris in a 4 years old female child making total number of reported cases to three. This patient underwent successful surgical management and is living a normal life.*

Key words: *Biliary ascariasis, Hepatic ascariasis, Liver abscess, CBD exploration, Sphincteroplasty, Hepatic perforation.*

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Introduction

Ascariasis is one of the most common helmenthic disease in humans.[1] It involves hundreds of millions of people in countries where the standards of public health and personal hygiene are low.[2] There have been numerous reports of surgical complications of ascariasis such as intestinal obstruction, perforation, volvulus, intussusception and common bile duct obstruction.[3-4] While biliary ascariasis is relatively common hepatic ascariasis is rare[10]. Hepatic perforation due to ascariasis is extremely rare and has been reported only on two occasions. Hereunder we present a patient of biliary ascariasis with hepatic ascariasis and perforation of the liver abscess by the ascaris and managed successfully by timely surgical intervention.

Case Report

A 3 years old female child, 2nd in birth order, product of a normal delivery was brought with complaints of pain abdomen of 15 days duration which was colicky in nature. There was history of vomiting for one day and it contained worms once. There was history of intermittent, high grade fever (102-103°F), associated with rigors, of one week duration.

On Examination child was febrile and irritable. Anaemia, cyanosis, jaundice and oedema were absent. Pulse was 100/minute and regular. Respiratory rate 24/minute and regular. Abdominal examination did not reveal any distension or mass. There was diffuse tenderness with guarding in the right-upper abdomen. Rest of the abdomen was soft. There was no organomegaly and no mass palpable. Bowel sounds were heard. No free fluid was noted in the abdomen.

Investigations revealed Haemoglobin (Hb) = 10.2 gm.; Total leucocyte count (TLC) = 12.5x10⁹/L.; Differential leucocyte count (DLC) = P75 L25; Platelet count 105x10⁹/L. Peripheral blood film (PBF) was normal. Bleeding time (BT) 1 min 15 sec., Clotting time (CT) 6 min 30 sec., Blood urea 25 mg%. Serum creatinine 0.49mg%, ALP 892 IU/L. Repeat ALP after one week 494 IU/L. Random blood sugar 105mg/dl SGPT 237, SR bilirubin 1.2 mg/dl, ECG all leads was normal, X-ray chest PA view was normal. Blood culture was sterile. Ultrasonography of abdomen revealed multiple linear echogenic shadows without acoustic shadowing in both extrahepatic and intrahepatic ducts. Common bile duct was dilated to 1.8 cms in size with multiple worms in it. Gall bladder was contracted. Other viscera were normal.

The patient was put on I/V fluids, nil orally, perentral broad spectreum antibiotics and her vitals were monitored closely. The patient showed remarkable improvement in her signs and symptoms. She was dewormed passed many worms with the stools and was doing well. On 6th day of admission she once again started showing spikes of high grade fever (102-103°F) with rigors and chills. The patient was subjected to repeat USG examination which revealed a liver abscess 3x4 cms in size in the right lobe with worms in it. Intrahepatic ducts, extraheaptic duct and common bile duct were dilated with multiple worms in them. Keeping in view the deterioration in the general condition of the patient, decision was taken to operate upon the patient. The patient was prepared and under general anesthesia the abdomen was opened by a right subcostal incision. Findings included a 4x4cm size abscess cavity on the anterior superior surface of the right lobe of liver being perforated by an ascaris, half of which was in the cavity and other half outside on the surface of liver. Pus was trickling from the mouth of ruptured abscess cavity. The abscess was opened up and 6-7 dead worms seen in the abscess cavity

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were removed. CBD was more than 2cms in size. Lot of adhesions were found around CBD. Multiple enlarged lymphnodes were seen around the CBD. All pus and debris was removed and cavity packed with omentum. Cholecystectomy was performed. Choledochotomy was undertaken and about 13 worms were removed from the common bile duct (CBD).

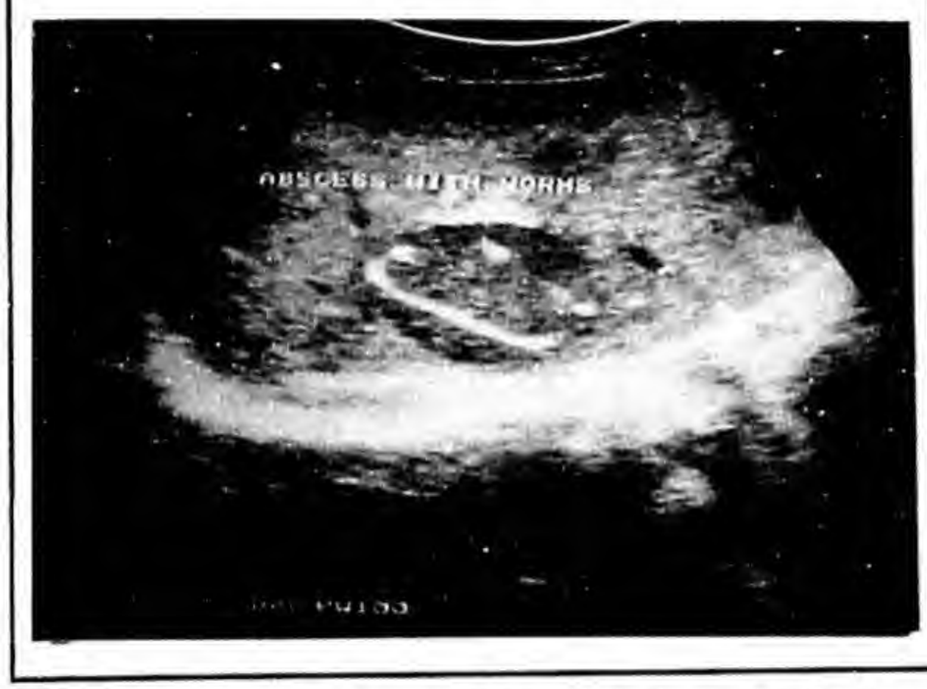

Fig. I. Ultrasound picture of hepatic abscess with Ascaris Lambricoides in it.

Many worms were removed from intrahepatic channels using stone holding forceps and saline wash outs. T-tube was put in the common bile duct and a transduodenal sphincteroplasty was fashioned to allow free drainge of infected bile and any left-over worm in the intrahepatic biliary channels. Post-operatively the patient's condition improved and she became afebrile. Orals were started on the 6th post-operative day. A T-tube cholangiogram on 10th post-operative day showed a free flow of dye down into the duodenum and visualization of both right and left hepatic ducts and CBD nromally. The T-Tube was removed on 11th post-operative day and the patient was discharged on 12th POD and was regularly followed in out-patient department (OPD). She is doing well now a year and and half from the date of surgery. The weight gain and change of skin colour to normal pink was spectacular. She is now symptom free, active and is undergoing normal schooling.

Review of Literature

Though roundworm infestation is a treatable condition, it is the surgical complications of these that are responsible for the associated morbidity and mortality. The commonest surgical problems that present as abdominal emergencies include intestinal obsruction, appendicitis, peritonitis, biliary and pancreatic ascariasis etc.[2,6,8,9] After entering the biliary tract through the ampula of vater, the worms freqently migrate into the liver parenchyma.[7] In few instances they may get arrested finally in the peripheral bile ducts in the liver. Although in heavy infestation the larvae that develop from ingested eggs in the small bowel may enter the systemic circulation bypassing the lungs and become embolized in organs, they are soon destroyed.[10]

Fig. II. CBD on exploration/packed with roundworms

Thus the only way the adult worm can reach the liver parenchyma in hepatic ascariasis is by way of the biliary passages. Adult worm can survive in the liver for up to a period of one month.[6] More often these worms may lead to formation of a single or multiple hepatic abscesses that may eventually rupture into the body cavities if not drained surgically[12]. Occasionally the worms that reach the liver parenchyma disintegrate after a period of time, releasing thousands of ova into biliary passages resulting in a suppurative cholangitis or granuloma formation.[13]

Since hepatic ascariasis follows biliary ascariasis, the symptoms and the course of both is almost identical. Initially the patient has acute colicky upper abdominal pain with nausea and vomiting. There may be no pyrexia or jaundice at the onset of symptoms. Once the infection sets in the patient becomes progressively ill with high, swinging temperature and the pain becomes more constant and localized to the upper part of abdomen. The liver is enlarged and tender and jaundice may be evident at this stage. There is leukocytosis with predominance of neutrophils. Essionphils may be absent.[10] Abdominal ultrasonography is the investigation of choice followed by endoscopic retrograde cholangiopancreatography (ERCP).[8] The accepted method of treatment is surgical drainage of hepatic abscesses.[5] Though hepatic ascariasis has been reported frequently, the perforation of hepatic parenchyma has been reported only in two patients, 3 and 5 years old girls both of whom died and findings were confirmed on autopsy.[11] However, in the case reported presently surgical intervention was carried in time with the drainage of liver abscess, CBD exploration with removal of all the worms from common bile duct and a sphinteroplasty. The patient had a uneventful recovery and continues to live without symptoms now one and a half year aftersurgery. Thus the

case was salvaged from a potentially lethal condition to full recovery.

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DEEP FEMORAL ARTERY INJURY FROM BLUNT TRAUMA - RARE PHENOMENA AND A DIAGNOSTIC DILEMMA

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Abstract: *Massive hemorrhage from the deep femoral artery (DFA) is an un-common entity in the setting of blunt extremity trauma without femur fracture. However it is not uncommon after penetrating trauma[1]. Blunt trauma causing deep femoral artery injury is nearly always accompanied by femur fracture[2]. Rupture of deep femoral artery from blunt trauma without femur fracture is a rare entity[3]. It creates a diagnostic dilemma, especially for a young and inexperienced attending surgeon. Massive hemorrhage and Pseudo-aneurysm formation with such injuries has been reported[3,4]. We report an additional case of deep femoral artery injury with massive hemorrhage, hemodynamic collapse and without femur fracture.*

Key words: *blunt trauma, deep femoral artery, fracture femur*

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Case Report

A 4 year old female child was brought to emergency ward after one hour of sustaining injury, in the state of hemodynamic compromise with feeble radial pulse and unrecordable blood pressure. She was hurt by a steel board which fell on her thighs during a religious ceremony. She developed cardiorespiratory arrest during the process of admission to the ward. She was thoroughly rescucitated by intravenous fluids, parentral adrenaline, endotracheal intubation and blood transfusion. She recovered and her thorough examination revealed hugely swollen, tender and bruised right thigh. Dorsalis pedis, posterior tibial and popliteal pulses were well felt. However the femoral pulse was difficult to palpate probably because of huge hematoma. After rescucitation base-line investigations were performed. Her Hb was 6 gms%, BUN: 43 mg/dl, Serum creatinine: 0.6 mg/dl, Sr. Na: 130 mmol/l and Sr. K: 4.3 mmol/l. Pelvic radiogram revealed fracture of inferior ramus of right pubis, intact right femur (fig.1). X-ray left lower limb revealed fracture of upper ends of tibia and fibula. Paracentesis abdominis was negative. Abdominal ultrasonography was normal Presumptive diagnosis of deep femoral arterial injury was made. After receiving 3 units of blood transfusion she was shifted to operation theatre in view of the progressively increasing swelling of right thigh and persistent hemodynamic instability. Exploration revealed a huge hematoma in the intermuscular plane extending upto the femur, normal superficial femoral artery

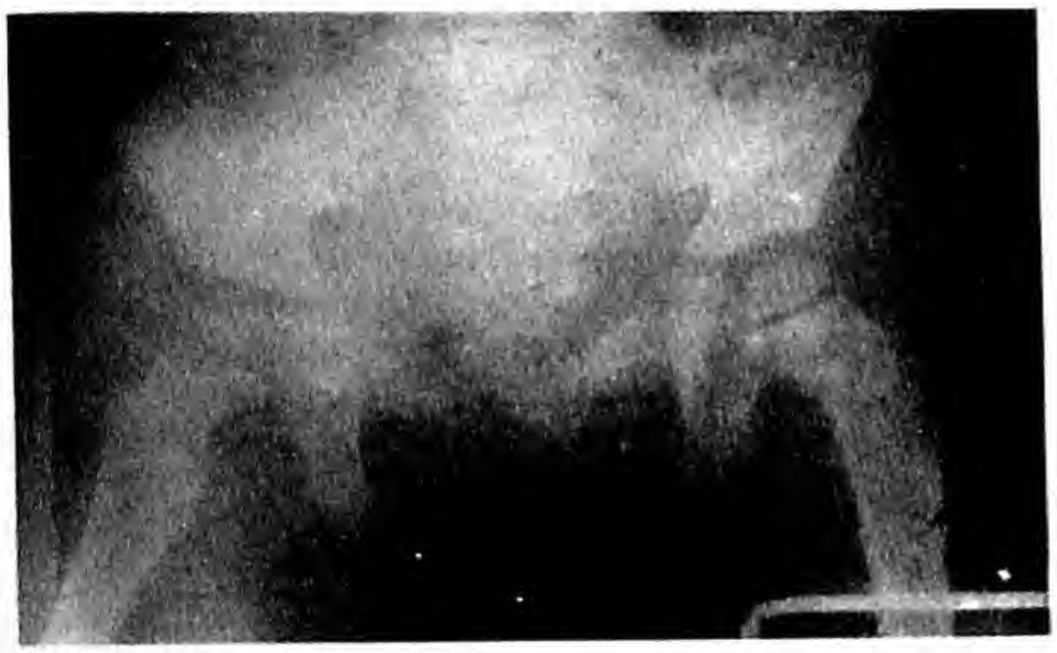

Fig. I X-ray pelvis (AP) revealing fracture inferior ramus of right pubis and intact right femur. Left lower limb has been splinted for fracture of fibula and tibia

Fig. II Right femoral angiogram revealing extravasation of contrast from perforating branch of deep femoral artery (DFA)

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and common femoral artery. However, the first perforating branch of deep femoral artery was torn and bleeding actively. The main trunk of deep femoral artery was intact. Per-operative femoral arteriogram with 60% urograffin displayed satisfactory flow in the common femoral artery and superficial femoral artery but extravasation of dye from profunda femoris artery (fig. 2). The hematoma was evacuated and the anatomy was well delineated. Surgical ligation of leaking perforating branch was undertaken. The femur bone was found to be intact. The wound was closed after fasciotomy and fracture of tibia and fibula managed by closed reduction. The patient was returned to intensive care unit and discharged on 5th day from the hospital without any neurovascular sequale.

Discussion:

Penetrating injury is usually responsible for deep femoral artery damage. Blunt trauma causing injury to deep femoral artery is invariably associated with fracture of femur. Presence of popliteal, femoral, dorsalis pedis and posterior tibial pulses does not rule out such injury. Hence an inexperienced surgeon should be aware of this possibility. Unexplained hypotension or shock and swelling of the thigh should raise the suspicion of such injury and mandates angiographic study. Angiography is invaluable in the management of such injury. It allows the surgeon to locate the site of injury and follow a specific mode of treatment. Blasier and Pape[3] reported 2 patients with rupture of deep femoral artery from blunt trauma that was not accompanied by femur fracture. Both had massive blood loss from DFA. In the first case a diagnosis of Compartment syndrome was suspected and fasciotomy revealed life threatening hemorrhage. Exploration and intraoperative angiography confirmed avulsion of three branches of DFA. In the second case with a similar presentation angiogram displayed an avulsed branch of DFA requiring intervention. Fasciotomy was also performed secondary to compartment pressure of 60mm Hg. Both patients required multiple transfusions. Lindfors et al[4] reported deep femoral artery injury with a late complication of pseudo aneurysm formation without femur fracture. This patient had suffered from blunt trauma thigh and had a huge hematoma, being managed conservatively during childhood and reported back during teenage with an acute swelling of proximal left thigh. Angiography revealed a pseudo aneurysm of 2nd perforator of deep femoral artery. Exploration confirmed the diagnosis and aneurysm was ligated and excised. Saletta and Freeark[5] used ligation, in five of their six cases. DeBakey and Simeone[6] reported 27 cases of deep femoral artery injury receiving ligation during World War II. They advocated routine repair in cases of injury to the profunda femoris artery. This is important in adults where chances of atherosclerotic blockade of superficial femoral artery are high[5]. However this was not relevant in our case.

Mueller et al[7] reported a patient with fracture of inferior ramus of right pubis and injury to deep femoral artery without femur fracture and persistent hypotension. Pelvic angiogram was normal but femoral angiogram revealed a ruptured branch of DFA. He performed embolization which successfully cured the patient. He recommended arteriography and embolization in all such cases of thigh compartment syndrome in which there is an unexplained need for blood transfusion.

Though it is a limited experience and since there is scanty data in the literature, we feel that any patient having normal pulsations with thigh swelling and hemodynamic deterioration, the situation should not be ignored. It warrants angiographic study and prompt surgical intervention. Embolisation is a viable option of treatment whenever possible.

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SOLITARY HYDATID SIGMOID MESOCOLON

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Abstract: *A 52 year old female reported in our OPD with complaints of chronic constipation and recurrent lower abdominal pain. Abdominal examination revealed a mobile, non-tender swelling in left iliac fossa. Patient was evaluated further. Ba-enema and sigmoidoscopy didn't show any intraluminal obstructioin of sigmoid colon. Ultrasonography of abdomen detected a cystic swelling in the left iliac fossa.*

Key words: *Hydatid, Sigmoid mesocolon, cyst.*

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Introduction

Hydatid disease is a cyclozoonotic parasitic infestation caused by larval stage of the cestode tapeworm, taenia echinococcus. Toxonomically there are four species of Echinococcus; E. granulosus, E. multilocularis, E. vogeli and E. oligarthus E. gramlosus is the commonest organism involved in human hydatidosis. The main organ involved is the liver, followed by the lung. No part of the human anatomy is immune execption being the avascular organs like nails, hair and teeth.

Man is an accidental intermediate host and is usually the dead end of the cycle. Nevertheless, there continues to be serious combat between the host and the parasite, and in the end, one or other must die. The definitive and intermediate host can not exchange their place in the cycle and at no time is there any organic connection between the host and the parasite. Echinococcus cannot settle or regrow on the epithelial surface.

Case Report:

A 52 years old married post menopausal woman presented with symptoms of recurrent lower abdominal pain and chronic constipation of six months duration.

Abdominal examination revealed a mobile, non-tender cystic swelling in the left illiac fossa. Margins of the swelling were freely felt and lower limit of the swelling was easily reached. There were no symptoms relating to urinary and reproductive system.

Patient was evaluated. Lower gastrointestinal study was normal. Ultrasonography abdomen revealed a signal cystic swelling in the left illiac fossa. Both ovaries were atrophied. Lt. kidney was found in its normal position.

Patient was taken up for laparotomy. Peroperatively a big single cyst located in the sigmoid mesocolon was found; Liver, Spleen, kidney, small gut and large gut were normal. Pelvic viscera were also normal. The cyst was gradually removed intact by separating it from surrounding mesentery and taking care of the vascular supply of the sigmoid colon. The cyst wall was found to be thin and clear fluid seen on opening the cyst. No daughter cysts were present in the fluid. The fluid was sent to laboratory for biochemical study and reported to be antigenic positive and having all biochemical evidence of the hydatid fluid.

Cyst wall on H.P.E. also revealed a thing laminated memberane.

Post operative period was uneventful. Patient is attending our OPD regularly and is doing well for last 2 years.

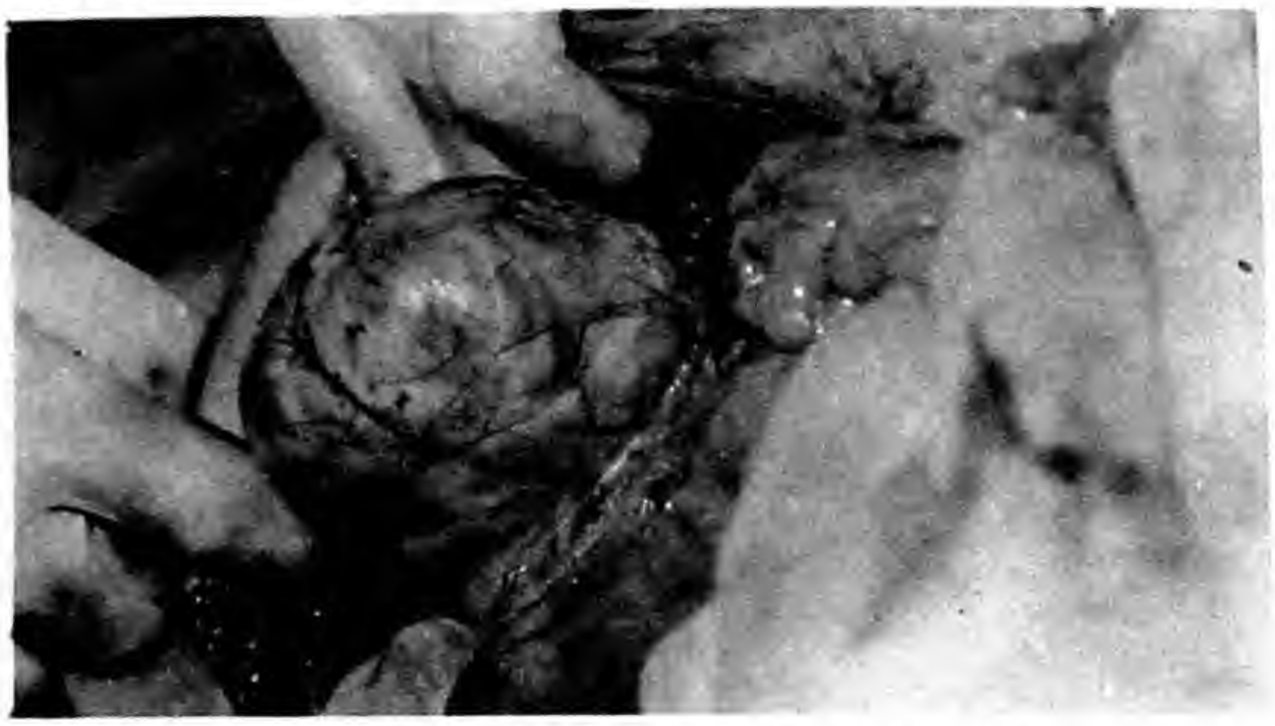

Figure: Cyst in the sigmoid mesocolon

Discussion:

In case of hydatidosis, liver acts as a first filter in 70-80% of cases, lungs for 15-20% of cases and next 5-10%

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through general circulation can settle any where in the body. In India, incidence of the hydatid cyst at unusual sites is higher as compared to other part of the world. Hydatid cyst at these unusual sites present difficulties in clinical diagnosis.

The symptoms of echinococcosis are those of a slow growing tumour; mostly being asymptomatic or having dull pain. In hydatid of sigmoid mesocolon constipation because of pressure was the presenting complaint in addition to dragging sensation in the left flank abdominal examination revealed a mobile, non-tender lump in the left illiac fossa.

There are no laboratory findings pathognomic of hydatid disease of sigmoid mesocolon. Eosinophilia can be detected in such patients but in our part of world that too in Kashmir valley, this is probably due to the fact that ascariasis is more prevalent. Now a day the most reliable diagnostic test uses partially purified hydatid arc 5-antigen in double diffusion test, but this facility does not exist in our hospital. Ultrasonography and CT Scan have very high diagnostic accuracy rates.

The hydatid cyst may get infected or rupture into the general peritoneal cavity. Although aspiration of hydatid cysts has been reported successfully; this modality of treatment is not usually recommended because of risk of disemination and fatal anaphylaxis.

Surgery remains the mainstay of treatment for echinococcosis. The cyst should be removed without rupture to reduce the chance of sending and disemination. The aim of surgeon should be to eliminate the disease with preservation of the vascularity of the colon.

Chemotherapy in case of the hydatidosis of sigmoid mesocolon is not favoured as there is no pericyst formation. There are reports that antihelminthics reduce the size of the cyst in some cases of hydatiosis, but these agents do not always give the satisfactory results and do have side effects like leucopenia, hair loss and hepatotoxicity. Most investigators use albendazole 10mg/kg body weight in cycle of 4 weeks followed by a drug free interval of 2 wks. Initially this was proposed to diminish the toxicity but another rationale for given albendazole in cycles rather than a continuous course is the autoinduction of its metabolism. The therapeutic level of albendazole. Sulphoxide, the major active metabolite in serum has not been defined, better absorption of albendazole when given with fatty meal has also been reported.

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HYPERTENSION OWING TO UNILATERAL RENAL HYPOPLASIA WITH RENAL CELL CARCINOMA

I.Shah M.S., F.I.C.S.; Rahul Gupta; C.L. Gupta M.Ch.

Abstract: *Hypertension owing to unilateral renal ischemia due to stenosis of main artery or its branches is well recognized entity. Lots of literature is available for hypertension associated with unilateral renal hypoplasia.*

Herein we report a patient in whom hypertension disappeared following removal of hypoplastic kidney, however the striking feature of the surgical specimen was diffuse hyperplasia of juxtaglomerular cells with Renal cell carcinoma in the lower pole of kidney.

Key Words: *Hypertenstion, hypoplasia, carcinoma, kidney.*

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Case Report

Forty five years male patient was admitted in the hospital with complaints of mild pain in the right lumbar area with history of blurred vision and occipital headache. patient also gave history of hypertension for last one year which used to fluctuate between 165/110 to 140/100 mmhg. At the time of admission patients blood pressure was 160/104mmhg. There was no history of genitourinary tract symptom disease. Patients hemoglobin and blood count were within normal limits with Sr urea of 22 and Sr creatine of 1.0, Na^+ 143 and K^+ of 4.3, urine microscopy showed few red blood cells and few casts. X-ray chest revealed cardiomegaly, per abdominal ultrasound showed small right kidney with left kidney hypertrophied. The findings of ultrasound were confirmed on I.V.U. with the addition that only faint nephrogram of right kidney was present (Fig. 1&2). CT angiography showed small irregular right kidney with right renal artery stenosis with normal left side.

An uncomplicated right nephrectomy was done through the bed of 12 th rib. Grossly kidney was small and irregular measuring about 6.5m and about 25gm in weight. Microscopically there was ischemic tubular atrophy with juxtaglomerular cell hyperplasia. There were polygonal clear cells with abundant cytoplasm which contained cholestrol and lipids consistent with renal cell carcinoma.

Discussion

In a study of atrophic kidneys associated with hypertension, Gifford and associates reported on twenty two patients with open arteries of small caliber supplying atrophic kidneys[1] and Emmett and associates reported on nine case[5], four of unilateral renal hypoplasia associated with hypertension and two of four patients who underwent nephrectomy were cured of hypertension[2]. Crocker and associates[3] used nephrectomy to cure hypertension in five cases exhibiting hyperplasia of juxtaglomerular cells in

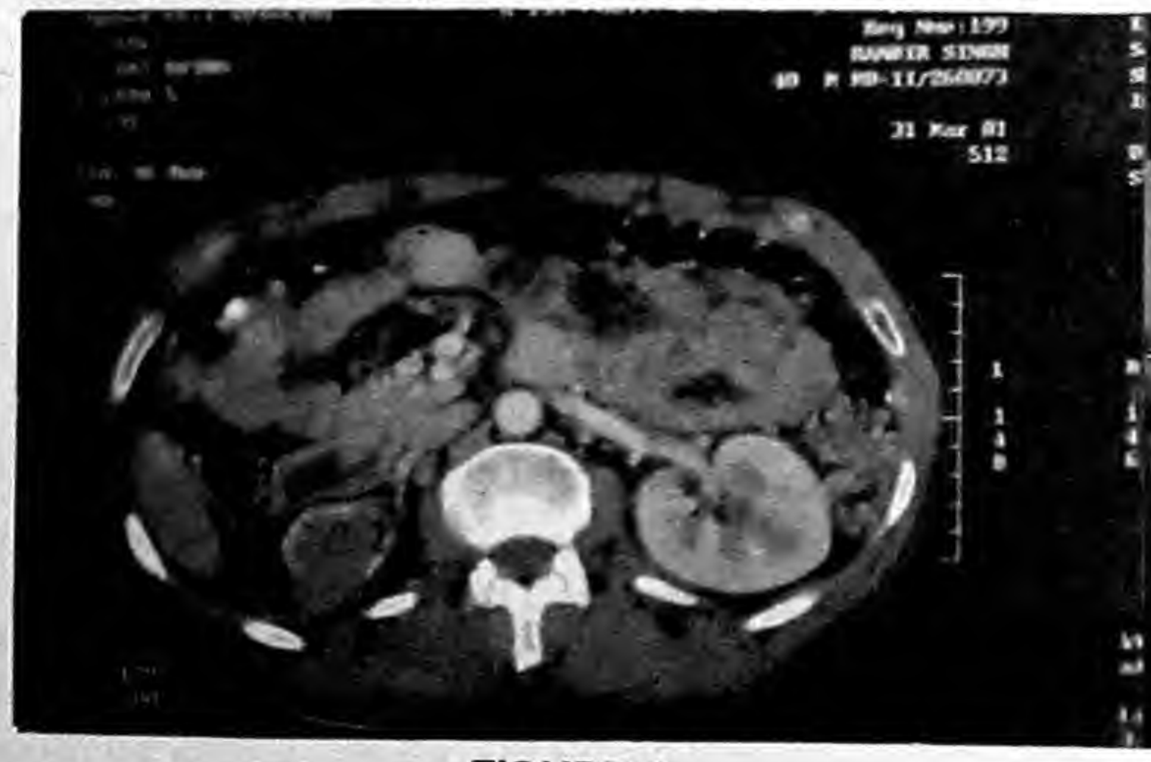

FIGURE-1

FIGURE-2

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hypopolastic kidneys that had small but unoccluded renal arteries[1], no other patholcgical lesion were noticed, but in our case report we want to highlight the fact that the literature is full with hypoplastic kidney and hypertension seen in our case, but a rare incidental finding of association with it was renal cell carcinoma which was detected only after the histopathological report of the specimen. This association is not mentioned in the literature.

The criteria used to divide patients into suspicious of renal tumors and in incidental groups are somewhat arbitrary but individual findings or combination of haematuria, flank pain, flank mass, fever, weight loss, and metastasis disease are well recognized presenting findings in renal carcinoma, which were not seen in our patient, except, hypertension. The criteria were broadened somewhat by CT Scan and ultrasound but in our case CT scan reported as small hypoplastic kidney with no suspicions of tumor although the cuts on scan were taken at 10 mm. Presenting symptoms like hematuria, flank pain and mass thought classical triad are late findings usually accompanied by advanced disease. Our case as well as those of others suggest that patients with incidently found tumor have lower stage disease and therefore better survival than patients presenting with recognized presenting signs and symptoms of renal cell carcinoma[3]. Hence in this case report we highlight that hypertension owing to unilateral hypoplasia with restoration of normal blood pressure after nephrectomy has been presented but at the same time the incidental finding of renal cell carcinoma in small kidney was noticed and it lays stress on the post operative evaluation of the specimens by histopathological examination which remains mandatory for all operated specimens even if there is clincially no evidence of malignancy.

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HERPES SIMPLEX ENCEPHALITIS

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Abstract: *Herpes simplex encephalitis is the commonest and the gravest form of acute encephalitis, seen sporadically throughout the year & in patients of all ages and in all parts of the world. It carries a mortality rate of 30-70% and those who survive are left with serious neurologic abnormalities. It is due almost always to Herpes Simplex Virus -I (HSV-I) which is also the cause of the common herpetic lesions of the oral mucosa. Rarely, however, do the oral and encephalitic lesions coincide. We report here a case of Herpes simplex encephalitis who presented with behaviour disturbances followed by seizures and coma and this patient had full recovery following acyclovir therapy.*

Key words: *Encephalitis, Herpes simplex virus, Siezures, Coma.*

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Case Report

A 29 year old female, presented with the history of behaviour disturbances of three days duration followed by generalised tonic-clonic convulsions. On the day of admission the patient was comatosed and only responding to deep stimuli. There was history of fever one week prior to the onset of illness which lasted for two days. Even on the day of admission, the patient had 3-4 episodes of generalized tonic-clonic convulsions. On examination, she was well built, married, with two children, with no anemia or jaundice. She was afebrile and there were no abnormal

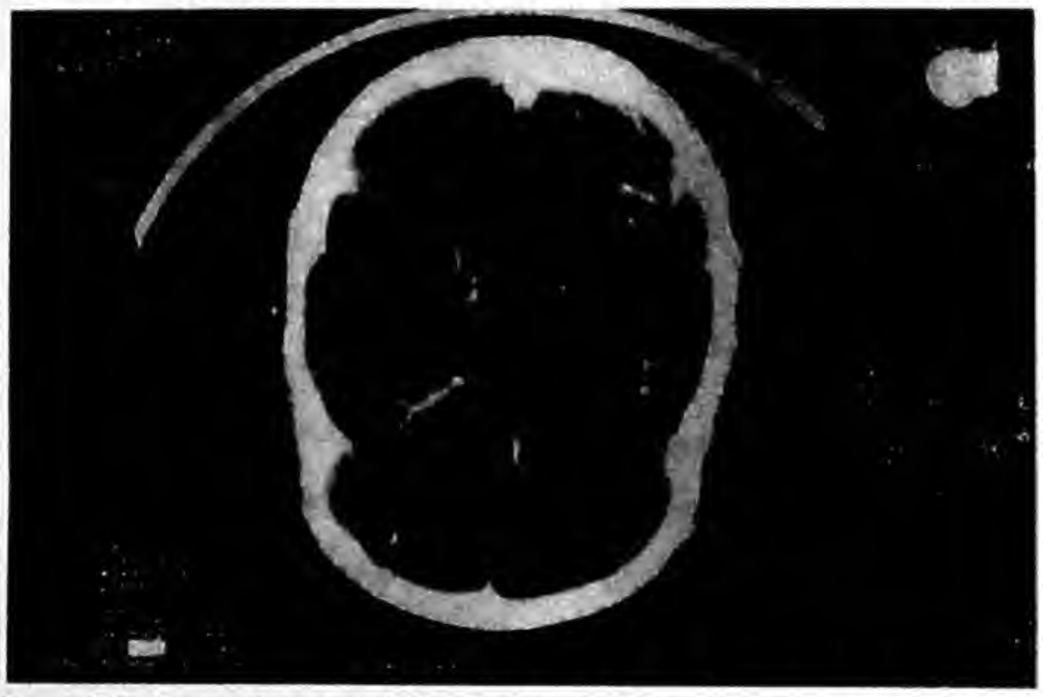

Fig. I C.T. Scan showing diffuse odema of brain more on right frontal and temporal lobes.

lesions over oral mucosa. She was comatosed and only responding to deep stimuli and at times very irritable and arousable too. She had bilateral papilloedema, pupils were equal in size and reaction to light was normal, was moving all four limbs and had no signs of meningeal irritation. Both planters were down going. A diagnosis of encephalitis was made and the patient was investigated on the following lines:

Routine investigations, BUN, hepatic function tests, blood counts and blood sugar were within normal limits. X-ray chest and E.C.G. were normal CT scan of head was done which showed diffuse oedema more on right frontal and temporal lobes with shift of ventricles to opposite side (Fig.1) MRI was also done which showed marked involvement of temporal lobe, right more than left consistent with the diagnosis of Herpes simplex encephalitis (Fig. 2). Gaurded L.P. was done under careful supervision. 5 ml. of C.S.F. was collected. it was under high pressure and showed 300 cells per cubic ml. and 90% were lymphocytes. Glucose content was 50 mg% and proteins were 200 mg % PCR was positive for herpes simplex encephalitis further confirming the diagnosis. EEG was

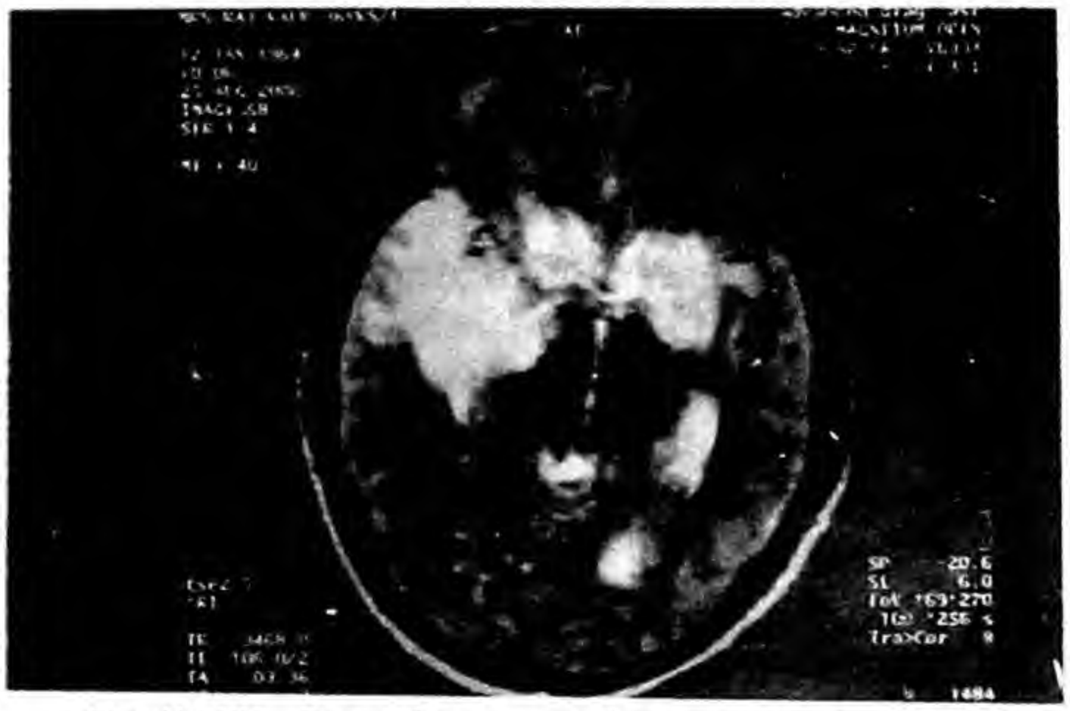

Fig. II MRI - Brain showing involvement of both temporal lobes right > left

done in later stages on 10th day of illness which showed diffuse theta & delta wave slowing.

Patient was managed with Ryle tube feeding, indwelling

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catheter, anticonvulsants, antioedema measures and was immediately treated with Acyclovir 10 mg./Kg body weight every 8 hourly for a period of 10 days. Each dose was diluted in 150 ml. normal saline and was infused in one hour's time.

Patient started improving by 3rd day of institution of therapy. Irritability was reduced. She had no more convulsions and by 5th day started responding to oral commands. By 10th day patient was up and above with oral feeding and full control of her bladder. She was followed up for 3 months. Patient has no neurological sequlae. At present, she is on anticonvulsants. Her papilloedema regressed and fundus was completely normal.

Discussion

Herpes simplex encephalitis is the commonest form of sporadic viral encephalitis. The cases are seen throughout the year and the age distribution appears to be biphasic, with peaks at 5 to 30 and above 50 years of age. Subtype 1 virus causes more than 95% of cases of HSV encephalitis.[1,2]

The pathogenesis of HSV encepthalitis varies. In children and young adults, primary HSV infection may result in encephalitis; presumably, exogenously acquired virus enters the CNS by neurotropic spread from the periphery via the olfactory bulb. However, most adults with HSV encephalitis have clinical or serological evidence of mucocutaneous HSV-I infection prior to the onset of the CNS symptoms. Reactivation of the latent HSV-I infection may be another mechanism for the development of HSV encephalitis.[3,4] Our patient was 29 years old female with no oral lesions.

The patients of Herpes simplex encephalitis present with fever, headache, seizures, confusion, stupor and coma. In some patients these manifestations are preceded by symptoms and findings that betray the propensity of this disease to involve the inferomedial portion of the frontal and temporal lobes. The later manifestations include olfactory or gustatory hallucinations, ansomia, temporal lobe seizures, aphasia, hemiparesis and abnormalities in behaviour. Very rarely an affection of memory can be recognised, but usually this becomes evident only later, in the convalescent state of the illness as the patient awakens from stupor or coma. Selling and herniation of one or both temporal lobes through the tentorium may occur leading to deep coma and respiratory arrest during the first 24 to 72 hours.[5,6]

Our patient present with behaviour disturbances, seizures and coma. Seizures were of generalized tonic-chronic type. The fever was only one week back and lasted for two days. The most important observation was that there were no sequale in this patient after she was started with Acyclovir on the 3rd day of her illness.

The diagnosis is made by M.R.I. and CSF examination particularly CSF polymerase chain reaction which has sensitivity of 95%.[7,8,9&10] Our case had CT scan of the brain which was showing only edema and shift of lateral ventricles but M.R.I. and CSF were diagnostic of the disease.

To conclude, Herpes simplex encephalitis is a common viral encephalitis. Early diagnosis and treatment can limit the sequlae. Even on the slightest suspicion, one should start the acyclovir therapy since this is the only encephalitis which has known treatment.

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HAEMANGIOPERICYTOMA OF NASAL CAVITY: A CASE REPORT

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Abstract: *Haemangiopericytomas have been classified as benign (low grade), boderline malignant (intermediate) and malignant (high grade) by Mac Master etal, 1975[1]. It has been suggested that haemangiopericytomas of sino-nasal tract manifest a more benign course than haemangiopericytomas of other sites[2]. The authors present a case of this tumor because of it's rarity.*

Key words: *Laemangiopericytoma, nasal cavity, epistaxis*

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Introduction:

Stout and Murray described Haemangiopericytoma for the first time in the year 1942[1,2,3]. It represents only one percent of all vasoformative tumors but an appreciable number (15-20%) occur in head and neck particularly in the soft tissues of the scalp, face, and neck[2,3]. Origin in sinonasal tract is less common, site of predilection being nasal cavity, spheno-ethmoid and ethmoid region[2].

Case report:

A 60-year-old male presented in the out patient department of the SKIMS Medical College Srinagar with complaints of progressive nasal obstruction, mainly on the right side with occasional epistaxis. Anterior rhinoscopy revealed a fleshy mass in the right nasal cavity above the inferior turbinate. It caused almost total airway obstruction and bled on probing. Posterior rhinoscopy and rest of the clinical examination were within normal limits for patient's age and so were the radiological investigations, which included X-ray of paranasal sinuses and chest. Mass was excised under general anesthesia and was seen to arise from lateral wall of nasal cavity above the inferior turbinate.

Pathology:

Gross: Fleshy fragments, together 25mm.

Microscopic: Microscopy showed an un-encapsulated tumor of round to elongated cells, around small capillary size and larger gaping vascular channels with hyaline thickening of the wall (Figure). Tumor cells showed vesicular nuclei and moderate ill-defined cytoplasm with pericellular reticulin. Mitosis was rare < 1/10 HPF and necrosis was absent.

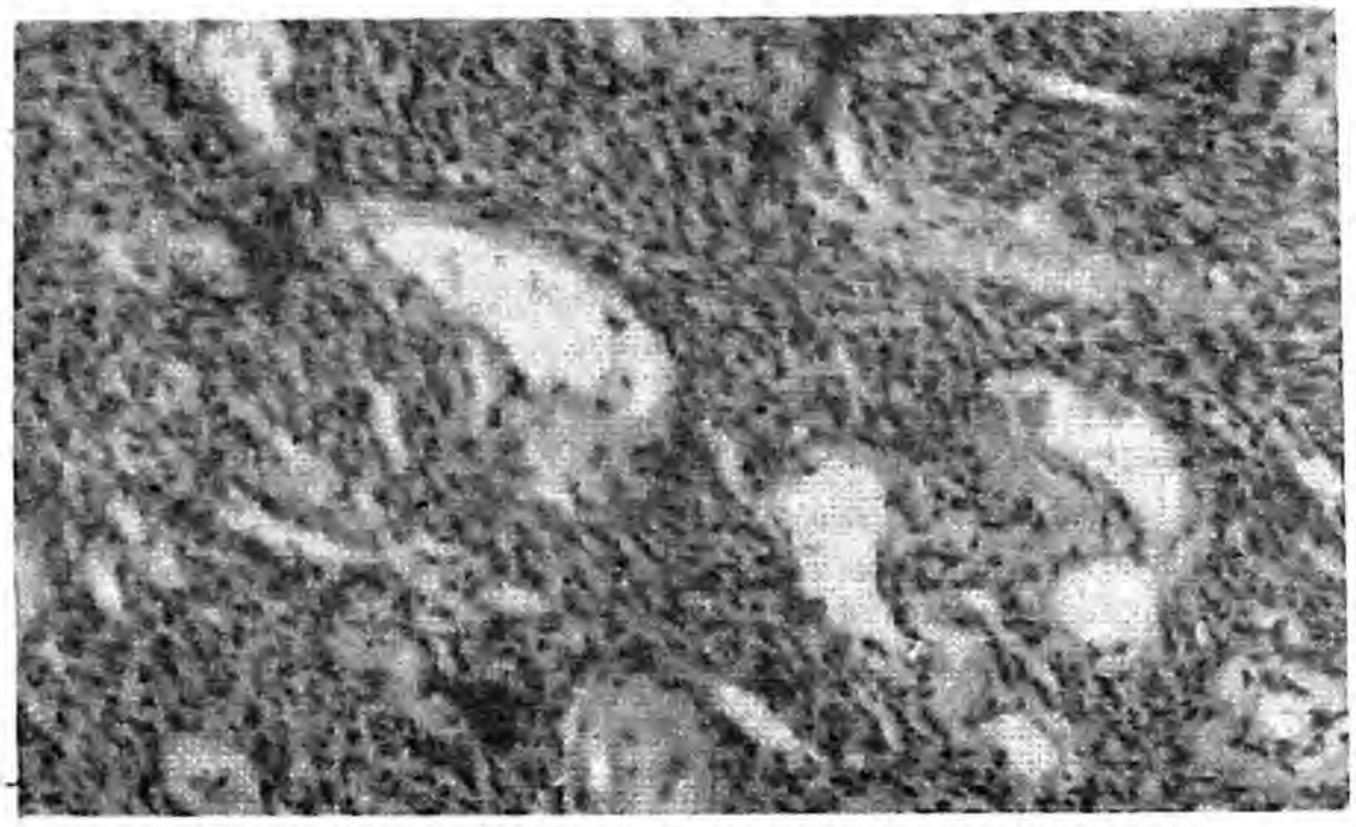

Figure. Photomicrograph of haemangiopericytoma nose. Hematoxyline and eosin x 400 showing vascular channels surrounded by pericytes.

Discussion:

Haemangiopericytoma is a tumour of the adult age, almost equal in both sexes[1,3,4], peaking in 5th and 6th decades[1,4]. Though it forms only 1% of all vasoformative tumours but an appreciable number (15-20%) occur in head and neck[1]. An origin in the nasal cavity, sinuses is relatively rare, the sites of prediliction being spheno-ethmiod or ethmiod regions.[1]

a) **Clinically,** a slowly expanding, solitary, asymptomatic mass is the general mode of presentation.[1] Symptoms occur when the site or size of lesion interfere with

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normal function. Pain occurs only in those lesions which are large and locally invasive, confined in unyielding spaces such as nose and para nasal sinuses where nasal obstruction and epistaxis are also frequent accompanying symptoms. The diagnosis is made only on biopsy.

b) **Pathologically,** the classification of intermediate or borderline haemangiopericytoma is necessitated because some cases do not fit into benign or malignant haemangiopericytomas. However, benign haemangiopericytomas out number malignant ones by a sizeable margin. Grossly, the tumours are soft and often tan in colour and usually present as a solitary fairly well circumscribed mass covered by a thin and richly vascular pseudocapsule, averaging 4-8 cms in diameter but lesions as small as 1cm and as large as 21cms have been reported.[1] Microscopically, the tumour characteristically consists of tightly packed cells around thin walled, endothelium lined vascular channels ranging from capillary sized vessels to large gaping sinusoidal spaces. The cells have round to oval nuclei measuring 7-13 mm in diameter and moderate amounts of cytoplasm with ill-defined borders.[1] The number of mitotic figures varies and is a helpful crition in predicting the biological behaviour and in distinguishing benign and malignant haemangiopericytomas. In majority of benign cases, fewer than 2-3 mitotic figures/ 10 HPF are present. Four or more mitotic figure/10 HPF are indicative of a rapidly growing tumour capable of recurrence and metastasis[1] along with occasional areas of heamorrhage and necrosis. The reported metastatic rate varies from 11.7% to 56.5%[1]. Most tumours metastasize within a period of 5 years after the initial diagnosis; but late metastasis, occurring 10 or more years after the initial diagnosis are not uncommon. The lung and skeleton are the frequent metastatic sites. Lymphonode metastasis is rare.[1]

Local excision seems to be the primary mode of treatment. More extensive surgery is required in less differentiated tumours that show features of malignancy as higher mitotic activity and areas of necrosis and haemorrhage. Radiotherapy and chemotherapy have been used in malignant tumours but need more substantiation in terms of pros and cons as the tumour, despite great vascularity, has been found to be radio-resistant. Radiotherapy therefore, has been reserved for inoperative metastasis or postoperative surgical fields.[3]

The tumour needs to be differentiated from other neoplasms with prominent vascular patterns as fibrous histiocytoma, synovial sarcoma and mesenchymal chondrosarcoma that mimic haemangiopericytoma which can be recognised by its uniform cellularity and vascular pattern and dense reticulin meshwork surrounding the individual tumour cells.

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RISK STRATIFICATION FOR ACUTE CORONARY SYNDROME-EARLY AGGRESSIVE INVASIVE THERAPY FOR WHOM?

Upendra Kaul

The term acute coronary syndrome (ACS) includes a spectrum of patients who present with chest discomfort with or without other clinical features caused by myocardial ischaemia. The underlying pathology of the ACS is plaque disruption of a minor stenotic lesion in majority of patients (70-75%) and plaque erosion of a more severe stenotic lesion in the remainder (25-30%)[1]. The possible sequale of plaque disruption can vary from an occlusive thrombus leading to acute myocardial infarction (AMI) to a subocclusive luminal thrombus in a disrupted fissure leading to unstable angina or a non Q wave myocardial infarction (MI). The event could at times be a benign one, leading to an asymptomatic small luminal thrombus or a silent occlusion of a severe lesion with adequate collaterals.[2]

The syndrome of unstable angina and non Q MI represents a formidable clinical problem. Besides the clinical presentation and electrocardiographic (ECG) changes it is now recognised that inflammatory markers such as high sensitivity c-reactive protein (CRP) and development of exquisitely sensitive biochemical markers of myocardial necrosis, including creatine kinase-MB (CK-MB), troponin i and troponin t are useful in the comprehensive evaluation[3-4]. These developments have made it possible to risk stratify patients of ACS into those with high risk of developing an adverse event (death, nonfatal myocardial infarction or recurrent ischaemia) or those who are at a relatively low risk for developing these complications.

Evaluation & Risk Stratification

A variety of risk factors contribute to the risk profile in ACS. Table I gives an overview of those risk factors. Multiple risk factors contribute to additive risk of adverse events in a linear fashion. It is therefore pragmatic to risk stratify the patients and design the therapy concordant with low, intermediate or high risk status. Various schemes and algorithms have been suggested to assist in this risk stratification.[5-8]

General Principles of risk stratification

Low Risk:

Subjects at low risk have a very good short term and long term prognosis. In general they do not need to be referred for coronary angiography. Appropriate medical therapy and coronary risk factor modification is usually successful. Low risk characteristics are described in Table 2.

Table-1: Risk Factors for adverse outcomes in acute coronary syndromes (ACS)

Profile at admission

- Age > 65 years.
- LV dysfunction (LVEF<40%)
- History of CHF
- Diabetes Mellitus
- Multiple coronary risk factors
- Prior revascularization
- Prior aspirin use
- History of angina on medical treatment.
- Ventricular arrhythmia during hospitalisation.
- Prior admission for ACS.
- ECG changes
  - St depression or elevation
  - T wave inversion.

Profile after admission

- ≥ 2 episodes of chest pain within 24-48 hours.
- Multiple episodes of chest pain.
- Recurrent/protracted chest pain on therapy.
- Positive CK-MB
- Positive Troponin
- Elevated CRP.

Most of these patiens should undergo stress testing before hospital discharge. Only patients with a significant ischaemic response should be subjected to invasive evaluation. Although a variety of agents including aspirin, heparin, nitroglycerine and beta blockers are variably used in practice but their role is very limited. Aspirin should be given to all these patients. Unfractionated heparin or low molecular weight heparin and glycoprotein IIb/IIIa blockers are not indicated. Patient with an ischemic response should

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be kept on beta blockers or calcium blockers and nitrates till coronary angiography is done.

Table-2: Low risk characteristics

- Age <50 years.
- Unremarkable coronary disease risk factor profile.
- No prior diagnosis of coronary disease.
- No recurrent rest pain >1 hr.
- No history of CHF & normal LVEF.
- No diagnostic ECG changes.
- Normal CKMB levels.
- Normal Troponin level.
- Clinically stable after admission without recurrent chest pain.

Intermediate Risk

Most intermediate risk patients have some high risk features. The value of percutaneous coronary interventions (PCI) and the utility of agents like unfractionated heparin/ low molecular weight heparin and glycoprotein IIb/IIIa blockers is not very clear though many major trials have included these patients for treatment. Table 3 lists the characteristics of this group.

Table-3: Intermediate risk characteristics

- Age - 50-65 years.
- Positive coronary heart disease risk factor profile.
- Prior diagnosis of coronary disease but no revascularization within past 6-12 months.
- Diabetes.
- Accelerating angina history.
- >1 episode of protracted chest pain.
- Some difficulty in controlling ischaemic pain.
- Abnormal ECG (nonspecific T wave changes, T wave inversion without ischaemic ST depression).
- Normal CK-MB, small Troponin.
- Normal Troponin T, small CK-MB.

These patients need admission to the coronary care unit (CCU) and the management has to be individualised. All of them should receive aspirin, heparin and anti ischaemic drugs. Patients who do not respond well or go on to high risk characteristics during observation need clopidogrel, Gp IIb/IIIa inhibitors and an early invasive strategy. Chest pain status, findings on electrocardiogram and biochemcial markers are the most powerful means of establishing intermediate risk. Patients who settle down promptly and do not have any recurrence of angina during the observation period of 1-2 days should undergo a stress test. Those with a significantly positive response need coronary angiography followed by PCI or coronary artery bypass graft surgery (CABG), if needed

Although pre-existing clinical featurs are useful for categorization in general, many ACS patients with adverse outcome present without any prior evidence of coronary artery disease or left ventricular dysfunction.

High Risk:

High risk patients (Table 4 for characteristics) should be aggressively instituted a combination of aspirin (100 - 325 mg once a day) and clopidogrel (300 mg loading followed by 75 mg once a day), unfractionated heparin / LMWH (superiority of LMWH is an unresolved controversy). The additional utility of clopidogrel therapy over and above aspirin in reducing he combined end point of death, myocardial infarction and recurrent ischamcia has been convincingly demonstrated in the CURE trial.[9] The benefit has also been seen in the group of patients who underwent early invasive interventions and were maintained on clopidogrel in addition to aspirin vis-a-vis patients who were only on aspirin[10]. These patients as per the trial results should also receive small molecule glycoprotein IIb/IIIa blockers (tirofiban or eptifibatide) if for logistic reasons invasive strategy cannot be undertaken within the next 24-48 hours[11,12]. Abciximab has not been shown to confer this advantage in patients who do not go for early invasive strategy within 48 hours[13]. Cannon et al[14] have recently demonstrated that patients of ACS in high risk category after administration of aspirin, dalteparin and tirofiban have a combined event rate (death, non fatal MI and recurrent ischemia) of 15.9% if any early invasive protocol with PCI or coronary artery bypass surgery as per the coronary anatomy is chosen as compared to 19.4% in the conservative (selectively invasive) strategy (p=0.025). The benefit role of glycoprotein IIb/IIIa blockers in reducing the combined end point of death, MI and recurrent ischemia during and after PCI is clearly established and all patients are recommended the use of these agents (abciximab, eptifibatide or tirofiban).

All patients in the high risk group thus need invasive evaluation followed by PCI or CABG if obstructive lesions are confirmed. FRISC II study[15] & TACTICS-TIMI[14] studies have clearly shown the superiority of early invasive strategy in this regard.

Risk Markers

Troponin:

Overwhelming data from several trials clearly support the key role for troponin i or troponin-t in risk evaluation of ACS[5-8]. The degree of troponin elevation is directly related to prognosis. These is no clear cut advantage of troponin t over troponin i. Approximately 30-40% of patients with troponin t or i elevation have a normal CK-MB level. Even if the ECG does not show ischaemic ST-depression abnormal troponin t and i clearly establish high risk.

Randomised clinical trials suggest that glycoprotein IIb/IIIa inhibitors and low molecular weight heparins have a particular benefit in patients with elevation of troponin t

levels more than 0.01 ug/ml.[13-17]

C Reactive Proteins

Recent data indicate that elevation of high senstivity CRP imparts an adverse prognosis in acute coronary syndrome[1,2,3,4]. However this marker of vascular inflammation is not yet recommended for clinical practice in decision making regarding the need for early invasive strategy for patient with ACS. A recent study however suggests that all patients with elevated CRP should be given statin therapy irrespective of their LDL cholesterol level[18].

Table-4: High risk characteristics

- Age >65 years.
- Prior admission for ACS.
- History of coronary disease (prior MI, stable angina).
- History of revascularisation particularly within the past 6-12 months.
- Diabetes.
- Multiple coronary risk factors.
- Prior aspirin use.
- Recurrent chest pain, espeically rest pain on aspirin, nitroglycerine and heparin.
- Refractory chest pain.
- New LBBB.
- CHF or LVEF<40%.
- Elevated CK-MB and/or Troponin.
- ECG: Ischaemic ST depression.

Electrocardiogram:

The presenting ECG plays a powerful role in the risk stratification. A normal or near normal tracing imparts low risk. ST depression especially >1 mm indicates an adverse prognosis. T wave inversion suggests a less severe prognostic abnormality than ST depression[19]. Patients with ST segment elevation should receive thrombolytic therapy or primary angioplasty.

In patients with ST elevation the combination of a fibrinolytic agent and a glycoprotein blocker, such as abciximab, has been elevated in dose finding and dose confirming studies[20-21]. The addition of full dose abciximab to half dose alteplase or reteplase resulted in nerly 80% of patiens achieving complete reperfusion at 90 min without a significant increase in side effects. Not only was patency improved but electrocardiographic signs of tissue perfusion were also significantly better with the combination[20]. However when this combination was tested in the dedicated GUSTO-V study[22], the combination did not have a better result on mortality reduction at 30 days, although it did lead to a consistent reduction in key secondary complications of myocardia! infarction including reinfarction.

The alternative to pharmacological reperfusion is coronary angioplasty which when used alongwith stent placement with adjunct abciximab therapy gives much better clinical outcome with a combined end point of death, reinfarction or urgent revascularisation of only 6%[23]. These are the best results reported so far in any trial of AMI management.

Approximately 10-15% of subjects with a typical ACS presentation and electrocardiographic abnormalities have non flow-limiting coronary disease or a normal coronary angiogram. Further more, on occasion ST elevation on initial electrocardiogram will evolve into a non-Q wave MI and not a transmural (Q wave) infarction.

TIMI risk score for unstable angina/non-ST elevation MI

In order to develop a simple risk score that has broad applicability and can be easily calculated making computer algorithms a simple scoring system has been evolved by Antmann etal[24] as a TIMI risk score for unstable angina and non Q wave MI.

The 7 TIMI risk score predictor variables are: (1) age 65 years or older, 92) at least 3 risk factors for coronary artery disease, (3) prior coronary stenosis of 50% or more. (4) ST segment deviation on electrocardiogram at presentation, (5) at least 2 anginal events in prior 24 hours. (6) use of aspirin in prior 7 days and (7) elevated serum cardiac markers.

Event rates at 14 days (Death, MI, or recurrent ischaemia necessitating urgent coronary intervention) increased significantly as the TIMI risk score increased. 4.7% for a score 0/1, 8.3% for 2; 13.2% for 3: 19.9% for 4; 26.2% for 5 and 40.9% for 6/7.

The TIMI risk score for unstable angina/Non ST elevation MI thus appears to be a simple prognostic scheme to categorise a patient's risk of death and ischemic events at the critical initial evaluation. Patients with 3 or more such risk factors need an aggressive management protocol which should incude administration of aspirin, clopidogrel, heparin (unfractionated or low molecular weight heparin) and should be subjected to an early invasive approach with the early use of glycoprotein IIb/IIIa blockers to have the best results at lowest risk.

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EFFECT OF FLUORIDE IONS ON THE PANCREAS OF GUINEA PIGS

It is an age of industrialization. rapidly growing industries have unfortunately resulted in a complex range of health problems due to environmental pollution. One of the most important health hazard resulting from environmental pollution is fluorosis. This disorder affects bones, teeth and soft tissues of the body. It is caused by cummulative action of fluoride products ingested over prolonged periods.

Ogilivie in 1951[1] observed the histological changes in the salivary glands of the rat following sod. fluoride administration, pancreas showed increased mitotic divisions of the alveolar cells and wider connective septa.

Oglivie (1953)[2] studied the histological changes of thyroid. liver, kidney and pancreas in experimentally induced fluorosis in animals. He observed in pancreas an increase in interlobular and intralobular connective tissue septa. The Mitotic activity of the cells was increased in majority of the experimental animals.

An autopsy study on 127 bodies was undertaken by Cell et al[3] (1965)[3]. Thyroid, aorta, kidney, lungs, brain, spleen and pancreas were studied histologically. The fluoride content was found higher in aorta than in any other soft tissue studied. An increase in fluoride content of aorta was found associated with calcification. Malm quest et al (1969)[4] found in the electron Microscopy study that rats fed with higher strength of sodium fluoride had accumulation of electron dense material in the mitochondria.

Henderson (1976)[5] stated that fluoride inhibited the oxidation of glucose by Islet of Langerhans isolated from rat pancreas. The rate of insulin biosynthesis was found more strongly inhibited by fluoride.

In the present study a total of 100 guinea pigs were taken and divided into four groups of 25 each. Group 'A' was given drinking water containing 10 ppm of sodium fluoride in one litre of water. The group 'B' received 500 ppm of sodium fluoride in one litre of water. The group 'C' was given 1000 ppm of sodium fluoride in one litre of water. The group 'D' served as control. The groups A.B,C and D were fed on standard diet. The animals were observed for changes in the gross appearance and body weight. The experimental animals and control groups were killed after 30, 60, and 90 days. The pancreas specimens obtained were processed for histopathological examination. Staining was performed by haematoxylin and Eosin stain.

The histological examination of the organ was categorised in A,B,& C groups. The groups A,B, & C were further subdivided into sub group. The group A and B showed swellings of the cells due to oedema and increased vascularity and increased connective compactness. The mean changes were seen in the group C. This group under microscopic examination revealed that the normal acinar pattern was disturbed. The cells lining the acini were oedematous. Islets were increased in number. The fatty infiltration was obvious. There was more increase in vascularity. The increase in connective tissue was and noticed at places. The acinar architecture was disrupted and cells lining the acini were more odematous in group. This group also showed the cells lining the acini with degenration changes.

Ogilvie (1953)[2] was the only poineer research worker to study the effect of fluoride in the pancreatic tissue. In 1951, he mentioned that the alteration of pancreatic structure was similar to that of the parotid gland of the rat. Subsequently in 1953, he observed that fluoride was associated with greater mitotic division of the alveolar cells and secondly with proliferation of connective tissue both in interlobular and intralobular septa. No significant proliferation in the islet cells were observed by him. Henderson et al (1976)[5] reported that the fluoride inhibited the oxidation of glucose by islet of langerhans isolated from rat pancreas. The present study was focussed to ascertain the changes regarding the various components of the pancreas with varying strength of sodium fluoride. The serous acini were broken and disrupted into 500 ppm strength and these changes were proportionally at 1000 ppm strength. Cells lining the acini showed initial oedema and later were associated with degeneration. The islet progressively increase in number with 500 ppm and 1000 ppm strength of sodium fluoride. With the higher strength of 1000 ppm, present study revealed increased vasculrity was associated with the fatty infiltration.

Over all effects of fluorine on pancreas is that of destruction of serous acini but with proliferation of islet cells. It can be deduced that exocrine functions are badly affected where as the endocrine functions are stimulated.

It can be postulated that damage to the exocrine function could affect the digestion of food and thereby indirectly causing loss of weight. A stimulation of endocrine functions of fluorine could also suggest its role as an antidiabetic agent. However. this postulation needs further investigation and confirmation.

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SPONTANEOUS RUPTURE OF HYDATID LUNG WITH HOOKLETS IN SPUTUM

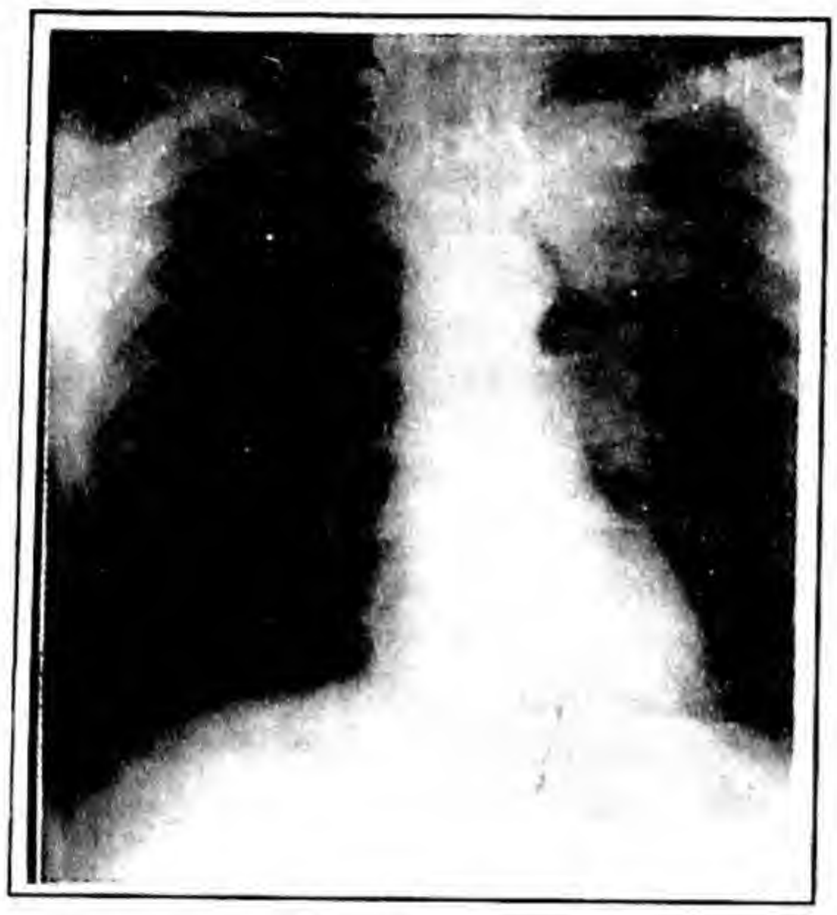

Fig.I: Chest X-ray PA view showing a well defined shadow in Left upper zone

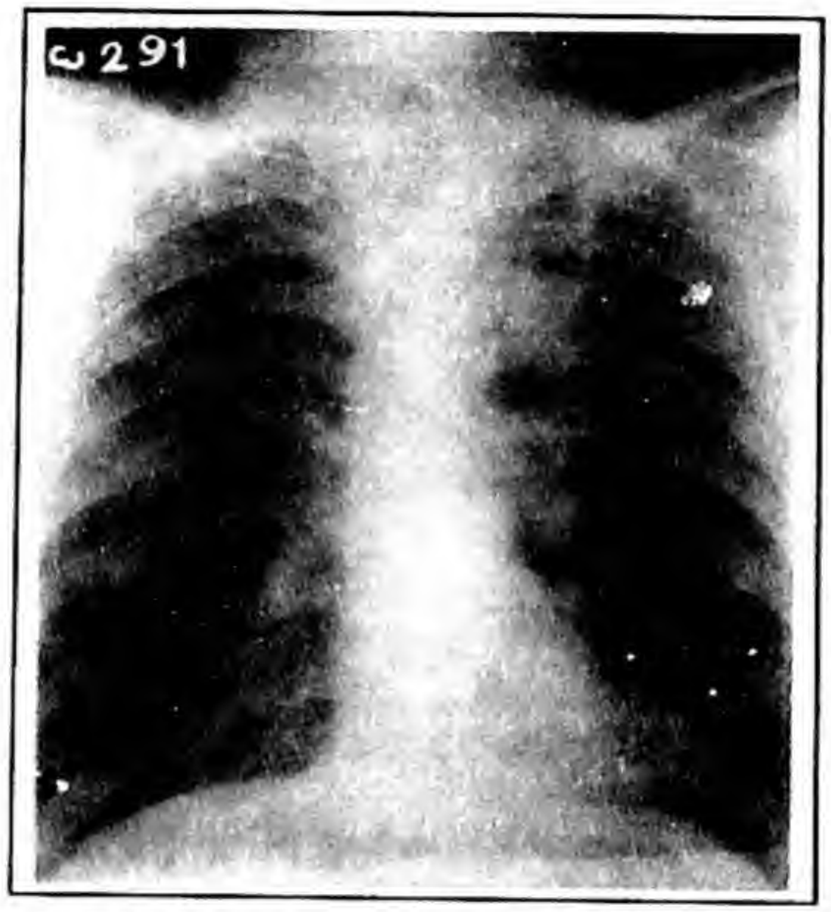

Fig.II: X-ray Chest-showing resolution of the shadow.

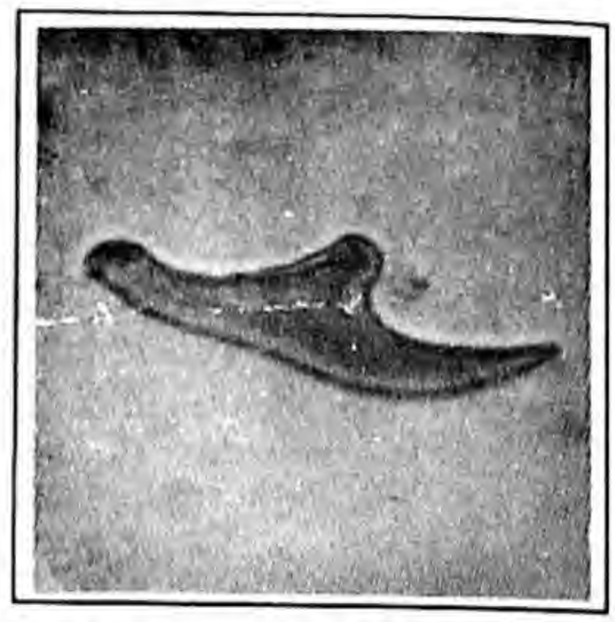

Fig. III: Hooklet from the sputum

50 years male patient was admitted with cough of 2 months. His chest x-ray revealed a well defined shadow (Left) upper zone (Fig. 1). He was admitted for evaluation. Patient next day developed salty taste, excessive expectorate with blood streaks. His repeat chest X-ray showed disappearance of the shadow (Fig. II). Sputum revealed hooklets of hydatid (Fig. III). Hydatid serology was positive. Patient had no allergic reactions secondary to spontaneous rupture of the hydatid. Patient was put on Albendazole.

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CORD PROLAPSE

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Umblical cord consists developmentally of the following components:

Ventral stalk, Umbilical blood vessels (two arteries and one vein)

Incidence of cord prolapse is one in two hundred advanced pregnancies .

Length of umbilical cord varies from 12 to 150 cms. With an average length being 18-24 inches i.e, 45 to 65 cms.

Definition: Descent of loope of cord beside or below the maximum diameter of the Foetal presenting part is called prolapse of umbilical cord.

Classification:

1: Occult prolapse.
2: Cord presentation (Fore lying cord)
3: Complete prolapse.

1: Occult prolapse: In which cord lies over the face or head of the foetus, but can not be felt on internal examination.
2: Cord Presentation: In which cord precedes the presenting part ,is held within intact membranes, and can be usually palpated through the membranes if cervix is patulous.
3: Complete cord prolapse: In which the cord descends past ruptured membranes ,and can usually be felt in the vagina or seen outside the vulva.

Causes: Descent of the cord is more likely to occur when the presenting part imperfectly fills the pelvic brim and the lower uterine segment.

1) Abnormal presentations like breech, shoulder, brow, face, transverselie, compound presentations
2) Multiple pregnancy (twins ,triplets, quadruplets)
3) Premature rupture of membranes prior to engagement of vertex or breech
4) Hydramnios.
5) Contracted pelvis ,cephalopelvic disproportion
6) Abnormally long cord (over 75 cms.)
7) Placenta praevia (battledore or velamentous type in which cord usually enters at lower lole of placenta.
8) Multiparity
9) Premature baby
10) When foetus is dead or dying , low pressure in the blood vessels reduces turgidity and it prolapse readily.

Essentials of diagnosis:

In occult prolapse incidence is unknown but quite common in about half of monitored labours, there were episodes of heart rate pattern consistent with diagnosis of cord compression. It is a temporary phenomenon particularly if the patient is shifted in a different position. In this type foetal bradycardia develops on firm fundal pressure .

In cord presentation pulsating loope of cord is felt through intact bag of membranes vaginally.

In cord prolapse a loope of cord is identified on vaginal examination or outside the introitus.

Compression of cord causes foetal hypoxia leading to violent foetal activity obvious to the patient, If the foetus is in good condition, auscultation shows marked bradycardia which develops rapidly during contractions, in scalp vein samples metabolic acidosis is demonstrated.

Risks and complications:

Foetus is in great danger of death by asphyxia from compression of cord between the presenting part and the pelvic wall or soft tissues and blood flow through vessels becomes obstructed. Rhodes in 1956 suggested that spasm of cord vessels is more important cause of foetal death than actual mechanical blockage. When cord is allowed to prolapse variation in temperature (low temperature) can lead to spasm , or any manure to replace or reposition the cord can lead to spasm of cord vessels. All this eventually enhancing the risks of the baby by metabolic acidosis. prematurity and birth trauma to suboxygenated fetus leading to overall foetal mortality of 40-50%.

Prognosis: Partial cord compression for less than 5 minutes period may not be harmful. Complete occulusion for same period or partial occulusion for a longer time will surely cause death due to CNS damage.

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Prevention of occurrence of cord prolapse :

Deferring of the artificial rupture of membranes until presenting part completely fills the pelvic inlet. Controlled and slow release of amniotic fluid should amniotomy be required when presenting part is high. If the membranes rupture spontaneously prompt vaginal examination to be done to rule out cord prolapse .

Treatment:

When cord pulsation's are entirely ceased and foetal heart sounds absent – the labour is left to terminate naturally as the foetus is dead.

In presentation of cord postural management such that the fundus of uterus lies at a lower level than the cervix to promote return of loope in the uterine cavity. This can be achieved by knee chest position but this posture is erksome and can not be maintained for more than 10 minutes. Another position is exaggerated sims position and raise the foot end of the bed . The greatest care is to preserve the membranes. Caesarian section is arranged if os is less than ¾ dilated (and with other indications for caesarian section) . If os is more than ¾ dilated with good prospects of emminent vaginal delivery , spontaneous vaginal delivery is awaited as soon as membranes rupture .

In prolapsed cord , when cord has not yet emerged from vagina , it is important to prevent it by vulval padding to avoid vasospasm. Other method of dealing this emergeny is described by Vago that full bladder inhibits uterine contractions . Technique is no. 16 foleys catheter with 5 ml. Balloon inserted into the urinary bladder and rapid infusion of normal saline by infusion set upto 750 ml. is done and cathter is clamped . This distended bladder keeps presenting part high which serves as first aid measure before preparing for caesarian .

Cord prolapse with fully dilated cervix (not otherwise complicated) needs immediate delivery by forceps if vertex or face is presenting and head has passed pelvic brim. Breech extraction is to be done immediately in case of breech presentation.

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DISEASE SURVEILLANCE IN KASHMIR ROLE OF THE DISTRICT HEALTH OFFICER. (DHO)

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Abstract: *In a decentralized set up the district health organization forms the backbone of primary health care delivery system and thus needs to be appropriately strengthened to cater to the needs of the ever-expanding rural health programme. Ideally, planning, implementation and monitoring of various health and family welfare programme are to be carried out at the district level. Information is every planner's raw material to build a system of effective surveillance for a correct community diagnosis, which culminates into the sequence of structuring objectives, determining priorities, and evaluating the programme efficiency and effectiveness. The degree to which a planner can succeed depends upon the degree to which he is able to collect, process, analyse, integrate and utilize the statistical data. District health officer is in a unique position of an administrator, manager, and epidemiologist, all rolled in one. Disease surveillance and programme evaluation are his main responsibilities, and the outcome of health care delivery in the peripheries depends on his dedication, efficiency and capability. The article discusses his role in strengthening the information and management system in a district, especially in the context of J&K State.*

Kew words: *District Health Officer, Disease Surveillance, Mini-surveys, Health Information System. J&K State*

Surveillance, defined as the continuous scrutiny of all aspects of occurrence and spread of disease that are pertinent to effective control, entails constant vigil and watchfulness over distribution and spread of disease and the related factors with sufficient accuracy and completeness to provide the basis for effective control measures. This modern concept of surveillance includes 3 main components viz;

- *Systematic collection of all relevant data on disease, deaths, health-related events and health-determining behaviours & practices,*
- *Orderly consolidation of these data, so that the raw data is transformed into useful information, and then*
- *Prompt dissemination of the results to those who need to know, particularly those in a position to take necessary action (as those responsible for prevention or control).*[2]

The sequence fairly suggests that the officer best suited for this purpose is the District Health Officer. He receives data regularly from the peripheral institutions and processes it on a continuing basis, and thus is among the first to understand its significance and pertinent message. He is the intermediate rank manager who has, on the one hand, immediate liaison with the medical officers and the community health officers of the district, and on the other hand, has direct access to the various disease surveillance, and control machineries of the headquarter for guidance, supervision or active assistance.

During the pre-independence era each district used to have a civil surgeon (meant for curative and administrative services, with assistant surgeons) and an epidemiologist (meant primarily for prevention and control of epidemics but also for some sort of disease surveillance). The Health Survey & Development Committee, appointed in 1946 under the chairmanship of Sir Joseph Bhore, recommended, for the first time, integration of preventive and curative services at all levels, and to facilitate it setting up of a unified health authority in each district[3]. All the subsequent committees appointed by the Government of India to give fresh recommendations on improving health care delivery upheld this suggestion, but it was the Kartar Singh committee, appointed in 1972 by the GOI to study and offer recommendations, among other things, on the structure for integrated services at the peripheral and supervisory levels, which suggested that an integrated setup was to be evolved at the district level with a Chief Medical Officer (CMO) and his deputies (Civil Surgeon, District Health Officer & District Family Welfare Officer), each deputy being incharge of one third of the district for all the health, family welfare, and maternity and child health programmes.[4]. The Kripa Narayan Committee, appointed by the planning commission further recommended that the district setup should be reoriented on the basis of the PHCs it comprises[5]. Health being a State subject in India, there is no uniform model of a district health setup, each state has

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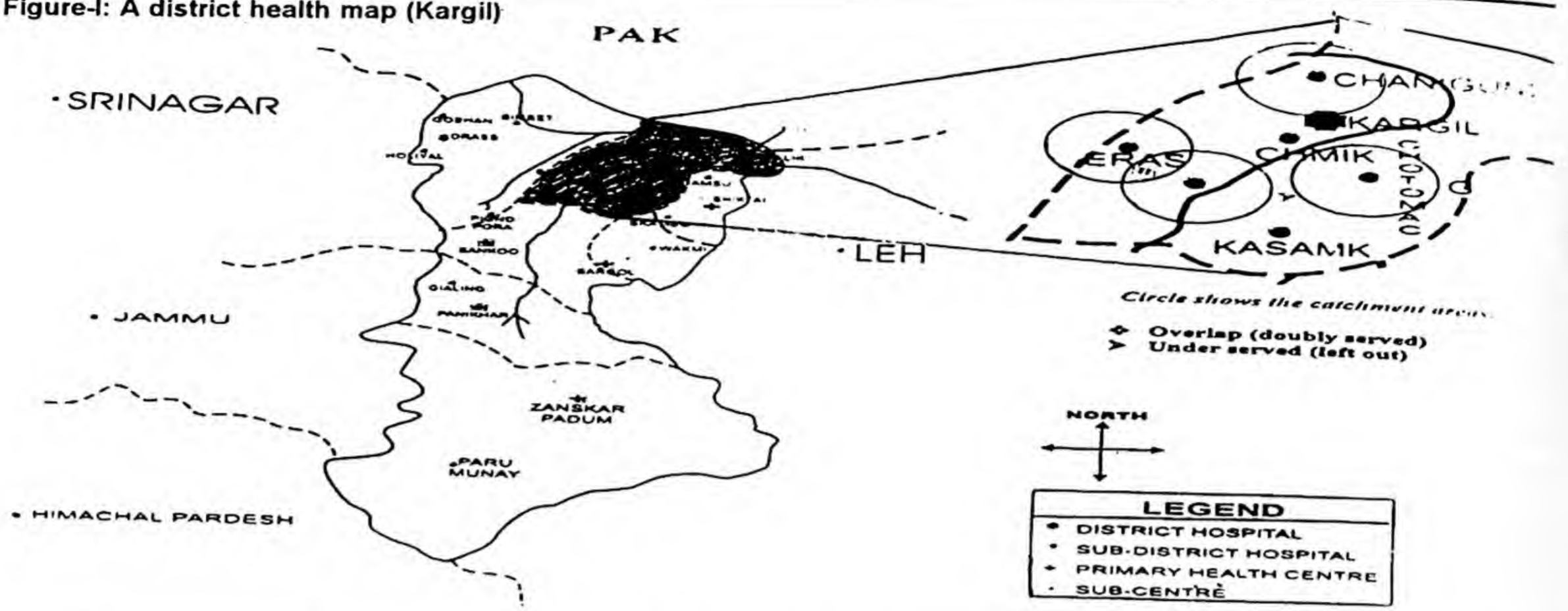
Figure-I: A district health map (Kargil)



developed its own pattern. The system adapted by the State of Jammu and Kashmir has a Chief Medical Officer assisted by a DHO (District Health Officer), a DIO (District Immunization Officer), and a deputy CMO. The former officer is envisaged to handle all aspects of health and disease and the latter is responsible for all the MCH & immunization activities. By convention the deputy CMO confines himself to the family welfare activities.

In the vast majority of cases the DHO is a senior medical officer who has passed many decades working, successively, as an assistant surgeon, medical officer, block medical officer etc, which has already provided him ample chance to acquaint himself with different aspects of health and disease at different levels of primary health care. He is consequently, supposed to be an experienced planner, adviser and supervisor within his district.

In a developed country, and even in most prosperous developing nations, where the job description of every manager and worker is clear with no ambiguity and no possibility of overlap, a DHO is amply clear that his sole or main responsibility is a continuous, constant, unceasing vigil on all aspects of heath and disease to keep public health problems under effective control and to predict, rather than be taken unawares, by epidemics and outbreaks. It has been pointed out that the DHO in his own areas has a unique opportunity for benefiting a community and contributing to the general epidemiological knowledge of the country[6].

Surveillance within a district should provide a broad assessment of specific problems in order to discern long-term trends and epidemiological patterns. Thus it provides the scientific basis for ascertaining the major public health problems in the area, there by, serving as a guide for planning, implementation and assessment of programmes for the control of various communicable and non-communicable diseases. Surveillance is also of paramount importance in recognition of acute problems, which demand immediate action. It means that surveillance is essential for proper assessment of priorities in public health.

Effective surveillance will depend on the synthesis of all the data derived from relevant sources, and the basic feature of this managerial tool is the mechanism by which pertinent epidemiological data are brought together to be analyzed, evaluated, correlated and interpreted by competent epidemiologists thereby providing the logical basis for effective action. The modern day control and eradication programmes place due emphasis on surveillance in making the initial assessment and in evaluating the progress of the programmes [1].

With surveillance being the prime responsibility of the DHO it is not out of place to expect that he should have, or get at the outset, as much information as possible about his district, which should include the physical environment and the demographic details and social, cultural, economic, ethnic, religious, and psychological background of the inhabitants. It is essential to obtain an accurate large-scale map of the district with every health facility marked in. If there were a mobile unit its visiting points would be noted. The epidemiologists recommended that a 5-10 km (or more or less radius), as per the available density or facilities) be drawn around each facility to delineate its catchment area (Figure 1). It will not only indicate the area or responsibility for each health facility but also show the left out parts vividly which may need immediate boosting or consideration for future developments[7]. All important roads, tracks, schools, panchayat buildings, tourist bungalows / huts, etc; and water resources, sources and reservoirs should be marked in. Details of factories, food

manufacturing/ processing units, food establishments, etc should also be indicated. Rivers and river basins should be highlighted prominently especially where such water bodies could isolate larger areas during floods, making access during floods / disasters impossible except through water or by air. In places like Kashmir Valley, where drinking water is generally delinquent and people living by the side of streams, rivulets, rivers and lakes use these generally highly contaminated sources as an alternative, special care has to be taken. Various outbursts of gastroenteritis in different districts leading to some preventable deaths show typical clustering in populations living on the banks of lakes and rivers using microbiologically unsafe water for drinking. The DHO catering to such an area should always bear in mind that the perpetual endemicity of water –borne infection with apprehension of periodic flare-ups, even alarming outbreaks, will remain there as long as people are not provided sufficient potable water and sensitized against use of lake or river water for drinking, cooking and washing etc.

Since the geographical terrains vary tremendously the DHO should acquaint himself with significance of different terrains and altitudes. There is a difference of 4000 ft in the altitude of Srinagar City (5100 ft) and Gulmarg (9000 ft), a mere 55 km away which has clinically significant bearing on variations in prevalence of respiratory, cardiovascular, gastrointestinal and even endocrinal disorders. The mountainous terrains pose a more formidable challenge, since in addition to height, difficult terrains with snow and cold temperature have to be overcome. The areas, which get cut- off because of natural compulsions, as excessive snowing, or due to man-made reasons, as border squirmishes, need extra-durable system of disease surveillance & outbreak control or rapid response systems, which should not succumb every now and then. A comprehensive system should be developed with viable pre-planned self-sustaining alternatives. It is a pity indeed, that in such vulnerable areas, health delivery and care systems should be so friable that for any outburst of gastroenteritis or pneumonia teams may be expected to air-dash; it shows a plain failure of the district health administration. Kashmir valley has so many areas, which are completely isolated from the main valley during winter (as Tangdar, Gurez) which need special season-proof surveillance systems.

Special challenges of disease surveillance in Kashmir

- Ambiguity of job description of various health professionals
- General lack of interest among supervisory, health education & extension education staff
- Lack of qualified/ trained surveillance officers & workers
- Trade unionism and politicization of health services at the peripheries
- Meagre community participation and non-committal community leaders and NGOs
- Non-cooperation of private practitioners and
- Near total breakdown of water-supplies especially during summers, and lack of routine quality control
- Ongoing turmoil

The customs, beliefs, attitudes and practices of people are more important to an understanding of health problems and usually much harder to uncover. The terrains of mind and heart are always more inaccessible than the most cumbersome mountainous villages. At the same time subjective perceptions in a community may be quite different from the objective assessments of the district health administrators. For example, although the endemicity of water borne infection is so worrisome to the health provider, for the majority of consumers its importance may be limited to its capacity to cause a flare up during summer months with disability and death. Sensitization of the community to their actual needs rather than demands (felt needs) may be required to keep the system relevant to health requirements of the community. The remains of primitive medicine and a staunch belief of various elements of the community (especially the decision-makers within the family or community) in empirical or unscientific practices is a very important deterrent to adequate sensitization. The attitudes to curses and evil spirits often provide an explanation for undiagnosed diseases or the bulk that goes unreported. There is always an important segment of the community which does not seek medical help at all or until there is an emergency. Women in general, and daughters – in-law in particular, may remain outside the purview of the normal statistics; same is true of the old, aged, invalid, very young, and of course, the very poor[9] This occurs in developed countries also – the Medical Research Council (MRC) of the United Kingdom found a much larger proportion of disease remaining outside the routine statistics (Table I). At the other extreme is the sizeable portion that visits the self-proclaimed practitioners of 'medicine' or spiritualism. It is probable that because of their well-designed publicity campaigns, of ignorance and illiteracy of our masses, and of the impotent Drugs-Act enforcement the major portion of sickness in our place is being tackled by those who keep it hidden from the regular surveillance systems. The private practitioners treat the major chunk of disease in urban areas, but they won't report the data mainly because of the haunting tax officials!

Gearing up the information systems at the District Level:

The routine statistics pertaining to health and disease

which is collected by the DHO should be useful to indicate the extent of various health problems (and their emergent nature, as epidemic potential), time trends, delineate high risk areas and high-risk groups, fill in the existing gaps in our knowledge (and if required to suggest types of surveys needed to provide additional information) and help in fixing priorities for action. For this to be possible it is essential that various baselines are handy for comparison. No situation or programme can be measured unless there are records with which to compare the current situation [11]. The DHO's office is supposed to collate and codify the pre-existing information, preferably in graphical form, for later reference. It is possible to detect upward trends and other significant changes only when corresponding data are compared with the fresh information. Cyclical changes in incidence may occur because of seasonal flare-ups (as with gastroenteritis including cholera); in others a slow change over the years may predict an evolving epidemic (AIDS). The build up of susceptibles to measles with a regular periodicity can easily be forecast from a progressive increase in reported cases, as has occurred in the valley during the last 3 years thereby alerting us to a possible measles epidemic in the coming years.

In areas where baseline data is not available (as in the J&K State) mini-surveys have to be conducted by the DHO's team to collect the background data. Currently such surveys are considered to be the most useful tools for establishing baselines[9]. It is no secret that, at present, absence of any baseline data is the main limitation for predicting trends and evaluating the fluctuations. Mini surveys can be simultaneously conducted over the whole district within a week, when planned, designed & conducted wisely. Where the DHO feels, he can get help from trained staff in the Directorate of Health for surveys & studies in his district.

Recording & conveying the information:

Currently the recording of the data, whether collected at the district level or sent in from the peripheries suffers from fallacious registration. The capability to maintain up-to-date registers, which are basically summaries of the general statistics, is essential for a DHO's office, which, in separate categories of diseases, should provide at least basic information on age and sex distribution, locality with useful details, tribal or ethnic categorization, preliminary diagnosis etc. It must be noted that laborious details of exact & detailed address, parentage's etc may be quite unnecessary except in cases where tracing of the patient later is essential, as in AFP, rabies, STD etc [6]. Specific registers for different chronic and acute diseases should be maintained. An attempt at collecting past information on TB in Pulwama and Srinagar revealed that the previous records were neither detailed nor meticulous. Other programmes also suffer similarly.

Table: I Action priorities in disease surveillance for the DHO

a) Preparatory action:
◆ Acquaint yourself with the geography, demography, sociology & culture of the area
◆ Prepare a comprehensive map with all relevant information including health outlets, water-resources, food establishments, factories etc.
◆ Learn about the psyche of inhabitants and their health-related attitudes and practices, and about the outlook of community leaders
◆ Acquaint yourself with the lower tier management especially those responsible for detection and notification, data collection and transmission, etc.
◆ Acquaint yourself with the high tier of management who directly or indirectly affect decision-taking, or provide formal/ informal support when needed
b) Direct surveillance functions:
◆ Assimilation & consolidation of data
◆ Analysis and routine reporting
◆ Investigation and confirmation of cases/ outbreaks utilizing epidemiological, clinical or lab methods.
◆ Feedback to the peripheral tier
◆ Feed –forward to the more central levels
◆ Routine monitoring of water quality and food quality in the district

Simple investigations:

In our situation it is most probable that perusal of the records and results of mini surveys will necessitate various types of studies (or plain investigations). At such a time the DHO should prioritise the problems so that arrangements are made to investigate the burning problems first. Evidently the endemic diseases with a potential for epidemic flare-up will be the first priority in the Valley. It has been recommended that the DHO should mount a properly conceived survey using his own personnel, and if he seeks help of a team from outside such teams should be of advisory, supervisory or assisting nature, and preferably the local workers and staff should be used for the actual study or survey. (6). Such workers are well versed with local problems, perspectives and priorities, and at the same time their active participation in well planned studies raises their own morale, establishes their credibility with the local populace and, above all, reorients them to newer methods, techniques and outlooks. It is doubtful if because of lack of training and experience any of the DHO's here can devise a well planned survey or study on his own. No doubt it is a specialized job needing a team of epidemiologists,

statisticians and public health experts to design a study but the DHO's team will ultimately have to put it into the field. The DHO facing a difficulty but desirous of doing a study or survey should get all possible technical help from the Provincial Directorate and that underscores the need for qualified and trained officers at the headquarter.

Table: II Difference between figures collected in routine surveillance and the actual suspected in a defined area, MRC Study, UK. (Information Gap)

Condition/Disease.	Suspected picked up by surveillance)	(Not Known (Picked up by surveillance)	passive	% of total detected by surveillance
1. Psychiatric Depression	125	12	9.60	
2. Glaucoma in persons 45+	27	3	11.11	
3. Women aged 45 or more with a diastolic BP over 100 mm.	131	24	18.32	
4. Conspicuous Psychiatric morbidity:				
Male aged 15+	90	32	35.55	
Females aged 15+	144	72	50.50	
5. Attempted suicide	6	3	50.00	

The District Health Officer is the pivot of disease surveillance activity within a district and is expected to focus his undivided attention on all aspects of disease surveillance and programme evaluation. As the middle-level management their role is very crucial in the entire management process but currently they are giving most of their attention to activities which are not commensurate with their job responsibilities, and that is the main reason behind the state of entire disease surveillance system being in disarray in J&K State. They need reorientation through regular regional meetings to have free exchange with their provincial colleagues catering to disease surveillance, various national schemes and epidemiology. In addition, quarterly workshops, for the DHOs and CHOs to orient, reorient and sensitize them to the importance and practices of an information system, statistical methods, epidemiology, sampling techniques, surveillance methodology etc, are a prime requirement For this purpose the DHO of districts could be reoriented even at national level institutes, provided they have an aptitude for surveillance work. This will go a long way in improving the disease surveillance and programme evaluation in the districts.

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DEVELOPING CARE AT DISTRICT LEVEL

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The achievement of sustained and equitable social development remains one of the greatest challenges facing the human race. Despite good progress over the past generation, more than one billion people still live in acute poverty and suffer seriously due to inadequate access to the resources —health services, education, infrastructure, land, and credit—required to give them a chance for a better life.

Coverage with the individual health elements of primary health care identified by the indicator 'local health services: population coverage' was as follows in 1991:

- Least developed countries: 69 per cent
- Developing countries: 89 percent
- Developed market economies: 100 per cent

About 1000 million people are estimated to lack regular acdess to local health services.

In South East Asian countries 50 per cent or more of the population do not have access to a minimum of health care. In India, the government estimates that today 75 percent of the population have access to at least first level of contact health care. This still means that 190 million people in the subcontinent do not have access to even that type of care.

In developing countries the extreme poverty of at least 45 percent of the people is the most crucial determinant of health needs. This very impoverished social class typically receives only about 10 percent of the national income. Governments have to take action to compensate for this inequality. If the redistributional actions of the government are not adequate, the goal of primary health care would only be attainable with a very low order of health service quality.

The challenge that exists today in many countries is to reach the whole population with adequate health services and to ensure their use.

The district is widely accepted as the nucleus (for the level of health systems management) where plans and budgets are prepared and implementation is coordinated with local government and with other sectors. The health management team continues to meet regularly to take decisions concerning the implementation of health programmes. The purpose of strengthening the health management process is to narrow the gap between policy and implementation, and to increase the confidence and skills of health management teams to improve functioning, which should cover the entire country to give a boost to management throughout the system and to develop a critical mass of health managers oriented toward problem solving.

Health care systems in India are represented by five major sectors or agencies which differ from one another by the health technology applied and by the source of funds for operation.

1. Public sector
   - Primary health care (primary health centres, subcentres);
   - Hospitals and health centres (community health centres, rural hospitals, district hospital and health centres, specialist hsoptials, teaching hospitals);
   - Health insurance schemes (employees state insurance, central government health scheme); and
   - Other agencies (defence services, railways).
2. Private sector
   - Private hospitals, polyclinics, nursing homes, and dispensaries; and
   - Clinics and general practitioners.
3. Indigenous systems of medicine
   - Ayurveda and Sidha
   - Unani and Tibbi
   - Homeopathy
   - Unregistered practitioners.
4. Voluntary health agencies.
5. National health programmes.

Primary Health Care

The government of India evolved a national health policy in 1983 keeping in view the goal of Health For All (HFA) by the year 2000. This laid down a plan of action for reorienting and restructuring the existing rural infrastructure with specific goals to be achieved by the year 2000. Steps are already underway to implement the National Health Policy objectives toward achieving HFA by 2000.

Health care must penetrate into the farthest reaches of

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rural areas, and everyone should have access to it. To implement this policy at the village level, the following schemes are in operation:

- Village health guides scheme
- Training of local dais, and
- ICDS scheme.

The village health guide is a person with an aptitude for social service and is not a government functionary. The health guides are mostly women. They come from and are chosen by the community in which they work. They serve as links betwen the community and the governmental infrastructure, and provide the first contact between the individual and the health system. They are trained in the nearest health centre for a total of 200 hours, spread over a period of 3 months.

After completion of the training, their duties include treatment of simple medical ailments and first aid activities, mother and child health (MCH) including family planning, health education, and sanitation. The health guides are free to attend their normal vocation. They are expected to do community health work in their spare time of about two to three hours daily, for which they are paid an honorarium of fifty rupees a month and drugs worth 600 rupees a year. There are more than 400,000 village health guides functioning in India.

Local dais (traditional birth attendants) are being trained to improve their knowledge of the elementary concepts of MCH and sterilization, besides obstetric skills. The training is for thirty working days, and is given at the nearest health centre for two days a week. On the remaining four days of the week they accompany the health worker (female) to the villages, preferably in the dais', own area. The emphasis during the training is on asepsis so that home deliveries are conducted under safe and hygenic conditions, thereby reducing maternal and infant mortality.

After completion of training each dai is provided with a delivery kit. She is entitled to receive a sum of two rupees per delivery. To each infant registered by her, she will receive three rupees. The national target is to train one local dai in each village.

Under the integrated child development services (ICDS) scheme, there is an anganwadi worker for a population of 1000. There are about 100 such workers in each ICDS project. At the present time 1800 ICDS blocks are functioning in India. The anganwadi worker is selected from the community she is expeced to serve. She undergoes training in various aspects of health, nutrition and child development for 4 months. She is a part-time worker, and is paid an honorarium of 250 rupees per month for the services rendered, which include health check-ups, immunization, supplementary nutrition, health education, non-formal preschool education, and referral services. The beneficiaries are especially nursing mothers and children below 6 years. Along with village health guides, the anganwadi workers are the community's primary link with the health services and all other services for young children.

Subcentre Level

The subcentres are the peripheral outposts of the existing health care delivery system in rural areas. They are being established on the basis of one subcentre for every 5000 people for the most part and one for every 3000 population is backward, hilly and tribal areas. Currently, 110,275 subcentres have been established in the country. The total requirement is estimated to be 138,000. Each subcentre is manned by one male and one female multipurpose worker. At present, the functions of a subcentre are limited to mother and child health care, family planning, and immunization. It is proposed to extend the facilities at all subcentres for IUD insertion and simple laboratory investigations which would go a long way in securing greater acceptance of IUD and early detection of complications of pregnancy. One female health assistant supervises the work of six female health workers.

Primary Health Centre Level

The health planners in India have visualized the primary health centre (PHC) and its subcentres as the proper infrastructure to provide health services to the rural population. The National Health Policy (1983) proposed reorganization of primary health centres on the basis of one PHC for every 30,000 people in the plains, and one PHC for 20,000 people in backward, tribal and hilly areas, for more effective coverage.

So far 16,535 PHCs have been established against the total requirement of about 23,000 by 1990. It is proposed to equip the PHC with facilities for selected minor surgical procedures and for paediatric care. In order to reorient medical education toward the needs of community care, three PHCs have been attached to each of the 106 medical colleges. The establishment of PHCs is the fruit of many years of grant effort to increase the outreach of the health services. (The Staffing pattern at a PHC is: one medical officer, one block extension educator, one health assistant (male), one health assistant (female), supporting staff-laboratory technicians, medical assistant and so on).

Community Health Centre (CHC)

To date, 1666 CHCs have been established by upgrading the PHCs, each CHC serving a population of 100,000 (one in each community development block), with thirty beds, and specialists in surgery, medicine, obstetrics and gynaecology, and paediarics with laboratory and X-ray facilities. For strengthening preventive and promotive aspects of health care, a new non-medical post called community health officer has been created at each

community health centre. The community health officer is selected from among the supervisory category of staff at the PHC and district level with a minimum of seven years' experience in rural health programmes.

Rural Hospitals

It is proposed to upgrade the rural dispensaries to PHCs and subdivisional hospitals to subdivisional health centres so as to cover a population of 500,000. These centres will have an epidemiological wing attached to them.

District Hospitals

There are proposals to convert the district hospitals into the district health centres. The current opinion is that the hospital should not remain 'an ivory tower of disease' in the community, but should take an active part in providing health services (including primary health care) to the community. Under the multipurpose worker's scheme, it has been suggested that we should introduce an integrated set-up at district level by having a chief medical officer (CMO) of the district with three deputy chief medical officer, with each deputy CMO being in charge of one-third of the district for all the health, family planning and MCH programmes. It has been suggested that the district pattern should be based on the number of PHCs.

The issues that need urgent attention are;

- Reaching the underserved population and under-privileged populations (increasing population coverage).
- Health system trend analysis as a basis for study of the implications of health policies.
- Measures for better coordination of various inputs.
- Preparation of a framework for national health development.
- Resource utilization review.
- Accelerating the health information system.
- Health care financing and economics.
- Leadership development for HFA.
- Quality assurance and self care.
- Looking for fresh, alternative approaches in order to ensure an effective framework and support effort directed toward HFA by 2000 and beyond.
- Health legislation (legislative support has an important role to play in improving policy formulation for guiding national health development and plans of action) - to review existing public health laws and suggest a unified, comprehensive health legislation for nationwide enforcement.
- Launching extensive urban development programmes (including health development for slum development for slum dwellers).
- Development and strengthening of district health systems.

Planning from the Base Upwards

To the consumer of health care, the advantages of access to specialist advice and modern technology are obvious. The disadvantages, of travelling, perhaps long distances, and being treated in unfamiliar surroundings can be equally obvious. The continued policy of concentrating resources within the grounds of the regional or teaching hospital will increase the size of the institution, the time spent in travelling, and probably the number of cases dealt with there.

Any change of this nature must rely largely on an effective system of primary health care which can filter patients through to the appropriate level. For these reasons, one of the most promising alternative strategies may be to think of planning the health services from the base upwards rather than from regional/teaching/district hospitals downwards.

It is essential to develop a sound and viable action programme on primary health care that can be used in training health managers, supervisors and workers at the district level and below. The application of management approaches for planning, organizing, implementation and evaluation at the district level is desirable. Issues such as integration of disease control programmes, sustainability and replicability of many successful innovations, importance of microplanning and decentralization need consideration to prepare strategies for strengthening the district health system.

The need for the maintenance and strengthening of referral facilities at the first referral level is becoming increasingly apparent. India has country wide programmes for expansion or maintenance of medical supplies and equipment.

The concept of voluntary health workers has increased the involvement of the community in health. It is important to review selection, training, deployment, supervisions, support and continuing education of those workers in order to help make necessary adjustments in national health policies. A district team problem-solving approach needs to be introduced as has been done in Thailand.

Management of the District Health System

The responsibilities of a district health authority include:

- formulating the district health plan;
- strengthening the district health structure;
- creating and developing the district team;
- integrating the different programmes and levels; and
- keeping under constant review the way in which the district works.

The district managment teams has to have a clear conceptual model of a district health care system. The team needs constant with the reality of the first level by including the health centre personnel in the team or through supervision activities.

District management must have the power (legal and administrative basis) to manage. There is need for a legislative enabling instrument to facilitate decentralization and a clear definition of responsibilities. The team requires a working relationship with the non-governmental organizations.

The staffing and equipment of many district hospitals are expected to improve toward the beginning of the 21st century, to give them even more weight in the organization of primary health care. But, care has to be taken to strengthen the periperal network simultaneously. Management tools and a conceptual model that clearly and adequately identifies the role of the hospital in the district are as important as the additional facilities provided.

Strengthening Health Management Systems

In order to narrow th gap between policy and implementation, to improve the functioning of individual health management teams and to develop a critical mass of health managers oriented toward problem solving, there is a need to strengthen the health management system in districts. Its approach to starting a sustainable process of management development is based on the actual working situation, and abilities and needs of the district staff. The district health management teams consist of officials with responsibility for specific health programmes (e.g., immunization, nutrition, environmental sanitation) and for particular cadres of staff (nurses, health inspectors and so on). The team is headed by a district medical officer (chief medical officer). Officials from the local administration (in decentralized systems) play an important role. The full management team should meet regularly to take decisions concerning the implementation of health programmes.

The team will tend to identify issues which cut across programme-specific barriers. Problems of financial management, coordination of transport, staff moral, and community involvement should frequently be selected for remedial action.

In strengthening the health management process, the most important work happens in the field, between the workshops, in putting the plans of action into practice.

The programme involves three modules. The start-up workshop includes sessions on problem identification, problem analysis, strategy development, and formulation of action plans. During the next three to four months these plans are implemented. The review workshop serves to assess the experience of participants in trying to implement their plans, and in analysing achievements and constraints.

Problem statements are reformulated, strategies reviewed and revised. The advanced review workshoop takes participants through another review and reformulation process and introduces them to a more comprehensive format for action planning. A final review meeting is held at the end of the six to seven months implementation period.

The complete process lasts about 15-18 months. The process proceeds from problems to stategies, and the emphasis is on practical ways of solving problems.

In Ghana and Laos, nearly all districts have begun to improve health services delivery and utilization, particularly with regard to financial management and uptake of immunization.

The strengthening district health system strategy requires teams to analyse day to day problems of programme implementation, plan how they are going to tackle those problems with their own resources, and criically review acheivements. The most important work happens in the field, between the workshops, in putting the plans of action into practice.

Management teams will be more committed to implementing plans if they are helped thoroughly to analyse and tackle problems that they themselves perceive to be important. Management and planning skills improve with practice and guidance. Teams build on initial achievements. New ideas are introduced as they become relevant.

Reaching the Underserved

There is a need for reorienting and restricting the health system infrastructure to reduce the existing imbalance by concentrating on the rural health infrastructure.

Priority must be given to underprivileged villages, urban slums and high-risk groups like infants, children, mothers, and so on, to improve their health status, using the PHC approach based on community involvement. This must include leadership development for HFA, quality assurance and self-care, integrated development for HFA, integrated comprehensive health services, and intersectoral activities.

The district provides an excellent organizational framework within which to introduce changes in the health system. At this level, policies, plans and practical reality can meet, and feasible solutions can be developed, provided human and material resources are made available and sufficient authority is delegated.

In order to succeed, primary health care must be strengthened by support from the top in the form of a clear, firm national policy, but its full realization depends critically on the people at the district level who are charged with the management and implementation of PHC strategies.

A suitable infrastructure is essential to implement integrated programmes. The organization of limited resources (human, logistic, facilities research) is essential.

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Against all odds

ZAFFAR A KHATIB
Executive Editor

"The search for a professional proof reader is proving to be as difficult as finding Osama bin Laden in the Tora Bora caves."

1994-2002 is just nine years-beginning of the ninth year of JK-Practitioner. I have been associated with the journal for the last six years or so, first as an assistant and now as the executive editor. When Dr. GM Malik approached me to work for him, I did not think the task would be as demanding as it turned out to be. My primary job of proof reading expanded in no time to overseeing the whole process of publication-from A-Z. In time I realized that I had to devote time, energy and patience in abundant measure to see the process through.

Some of my friends witnessing my pre-occupation advised me to call it a day. Reason I was not getting due recognition for the hard work I put in. I am not ambitious (not the best of the quality) and "recognition". may not mean much to me. The power of hiring and firing is best left to somebody else. I will make a mess of it. Others advise me to quit as this kind of labour was not financially a viable option. It may be true that the honorarium. I am entitled to as executive editor is not enough to pay for my gasoline bills which I incur on the job. If it was for financial gains, I would not have accepted the responsibility in the first place. Some things in life are beyond money. Still others tempt me with offers to start a similar thing. Six years addiction with "JKP" is strong enough to spurn their advances.

Let us go back to where we started. 9 years = 30 issues, is not an equation that would take, "time, energy and patience." True enough, but in normal circumstances. Things which you take for granted elsewhere are difficult to locate here. The working day is effectively reduced to 2 hours due to power shutdown. Deadlines are meant to be broken not honoured. Tomorrow means after a week. The search for a professional proof reader is proving as difficult as finding Osama bin Laden in the Tora Bora caves. When the final script is ready it has to be carried 700 miles away for offset printing. From then onwards you have no control over what you get back as a finished product. You have no control over colour combinations, no control over quality of photographs, no control over "reprint" reproductions.

With this background scenario, every issue is a cause for celebration. Not to miss an issue all these years is an achievement.

We have a lot to improve and hope to overcome the road blocks in our own indigenous ways. Pray for good times.

zakhatib@vsnl.net

7th National Conference on Bronchology in conjunction with the International Conference on Bronchology & Respiratory Diseases jointly organised by American Association of Bronchology, American Thoiracic Society, World Association of Bronchology, Japan, and American College of Chest Physicians, South India Chapter, 8 to 10 February at Hyderabad. Contact: Dr. Ajit Vigg, Organising Secretary, ICBRD - 2002 Tel: 040-323 0729/324 2971; Fax: 324 2971; Email: ajitvigg@hd1.vsnl.net.in Website: www.icbrd.com.

International Critical Care Congress 2002 and 8th Annual Conference of the Indian Society of Critical Care Medicine, 13 to 17 February, at New Delhi. Contact the organising Secretary: Dr. Rajesh Chawla, Room No. 1002, Free OPD, Indraprastha Apollo Hospitals, Mathura Road, New Delhi 110 044. Tel: 011-692 5801. Fax: 011-682 5584. Email: drchawla@vsnl.net; Website: www.criticalcare2002.com.

8th International Congress on Assisted Reproductive Technology and Advances in Infertility Management, 215 to 17 February at Ooty. Pre-congress workshop on Advanced Gynaec endoscopy on 13 February and on IUI/IVF/ICSI on 14 February at Coimbatore. For details contact Dr. Asha Rao, Rao Hospital, Coimbatore 641 002 or the Indian Society for Assisted reproduction, Flat No. 23-A, 2nd Floor, Elco Arcade, Hill Road, Bandra (W), Mumbai 400 050.

8th Training Course on Immunodiagnostics for Infectious Diseases sponsored by the Department of Biotechnology, Mahatma Gandhi Institute of Medical Sciences (MGIMS), Sevagram, 25 February to 2 March. Contact Dr. B.C. Harinath, Director, Professor and Head, Department of Biochemistry, JB Tropical Disease Research Centre, MGIMS, Sevagram (Wardha) 442 102 Email: jbtdrc@nagpur.dot.net.in.

Rewind 2001

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1. 187th Central Working Committe Meeting of Indian Medical Association (IMA) in progress at SKICC, Srinagar May, 2001 L to R.: Prof. Ketan Desai (President IMA), Dr. Sanjeev Malik (Secretary General) Dr. P Gogia (Joint Secretary), Prof. GM Malik (President State Branch of IMA) Dr. Mir Nazir (Secretary State Branch IMA) and Prof. A Rouf (Principal GMC, Srinagar)
2. Dr. Farooq Abdullah (Hon. Chief Minister J&K State receiving the guests at Dachigam, Srinagar, Kmr. (IMA meeting).
3. WORLD AIDS DAY at SMHS Hospital, Srinagar.
4. CME in progress at GMC, Srinagar Prof. A Rouf (Principal) introducing the speakers of the day, Prof. Farooque A Khan and Prof. Arfa Khan (seated). At extreme right is GM Malik (Chairman Academic Committee, GMC, Srinagar)

NATURAL HISTORY AND PREVENTIVE TREATEMENT OF RECURRENT MOOD DISORDERS

Subhash Chandra Gupta, DPM; Vinod Kumar Sinha DPM, MD; Soumya Basu ,DPM;

Introduction :

At least 12% of adults will suffer from some mood disorder at some point in lifetime with prevalence rate being 10-18% for major depressive disorder and 1-3% for bipolar disorder[1]. Considering the relapsing and remitting course of the recurrent affective disorder and the vast amount of research work that has been done in this area, it was thought to be pertinent to briefly review the salient features of the natural history and the various preventive treatments of recurrent mood disorders in this article.

NATURAL HISTORY OF BIPOLAR DISORDER

ONSET

The modal age of onset of bipolar disorder ranges between 15 and 25 years (that for major depressive disorder about 10 years later)[2]. However the age of onset of both disorders have decreased over past four generations[3] and earlier its onset also are associated with greater lifetime incidence and higher rates of recurrence[2]. Studies on age of onset in bipolar I and bipolar II patients have given wide ranges with a mean age of 28 years for bipolar I disorder and 26 years for bipolar II disorder[4] but other studies have shown no significant difference between the two[5]. Regarding onset and switch of polarity from depression to bipolar disorder, in a review[6] it was estimated that 10% of depressed patients developed mania while another study reported that only 5.2% of initially non bipolar patients developed mania during 10 years of prospective follow up[7]. Some workers have suggested that 1% change per year from unipolar to bipolar can be expected[8]. Another interesting study showed that bipolar patients have same rates of recurrence throughout the illness irrespective of at which episode or at what time their first manic episode occurred (as if these patients were predestined to become bipolar)[9].

For depressive patients, young age of onset, psychomotor retardation, guilt, high familial loading of affective disorder and family history of mania has higher risk of developing mania[6].

The proportion of bipolar patients who begin their illness with mania rather than depression varies widely across reported cohorts—34% in one study[10], 79% in another[11], and the balance of literature indicates that mania occurs in over half of the initial attacks in bipolar patients.

Several studies have shown that there are clinical differences in early and late onset bipolar disorders. Early onset bipolar patients have more psychotic symptoms, more manic episodes, higher level of co morbidity (with panic disorder, conduct disorder, and drug addiction), more number of mixed episodes and poor response to lithium. Several of these findings such as higher proportion of manic episodes and poor response to lithium in early onset bipolar disorders have been refuted by other studies (12).

LONG TERM COURSE

About 10% of those with bipolar type I disorder never suffer a major depressive episode. Overtime, a subset of type II disorder shift subtype diagnosis because of onset of mania and similarly some cyclothymias shift to other major bipolar subtypes. Nevertheless, bipolar II disorder and cyclothymia should not be viewed as simply transitional diagnosis and most patients with these disorders do not develop full blown bipolar I illness[13].

Initial studies found patients to be stable for a long time after a single episode. In most of the more recent follow up studies however, the single episode course is rather the exception. One view is that contemporary treatment may bring about symptom free periods which are less stable than those which occur more naturally with simple passage of time. Lundquist, 1945, noticed relapses were no more likely after a second episode than after a first episode while others have found tentative evidence that episodes cluster over time[14]. Regarding predictors for relapse or recurrences, very few studies have examined this factor in bipolar illness. Recent studies show that individuals with bipolar disorder tend to receive less social support than medically ill or non disturbed populations[15] and suggest that social support does influence course with low social support predicting greater number of weeks of symptoms across the year following hospitalization[16].

Epidemiological studies have found that 29% of bipolar patients admit to at least one **suicide** attempt in their life time[17]. A stress diathesis model was proposed[18a] the stressor being an affective episode or another stressful life event

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and the diathesis was reflected in a past history of repeated suicide attempts, elevated life time levels of aggression, impulsivity, comorbid cluster B personality disorders and a family history of suicidal behaviour.

Regarding **gender differences**, bipolar disorder occurs as frequently in males as in females[1], with no significant difference in bipolar I and bipolar II diagnosis in both sexes. Also, no significant gender difference has been observed in age of onset, number of manic or depressive episodes & number of hospitalizations[18b].

Rapid cycling affective disorder: This term is used when a patient with a bipolar disorder suffers four or more episodes in a year. It is found in 5-15% of bipolar affective disorders. Onset is generally in adulthood, but recent evidence points towards its occurrence in adolescents and in children also. It is seen more frequently in females with strong family history of bipolar disorder, associated with high risk of suicide, resistance to lithium therapy, hypothyroidism, certain neurological conditions (multiple sclerosis, head injury) and antidepressant treatment.A recent study from North India reiterated these findings (19).

NATURAL HISTORY OF UNIPOLAR ILLNESS COURSE AND PREDICTORS

Fortunate minority (30-40%) has a single lifetime depressive episode having few long-term sequelae. More often, major depressive episodes recur with increasing frequency. In fact, after second episode risk of third is about 70% within 3 years[20] without prophylactic treatment. The average depressive episode lasts about9-12 months without treatment, although about 20% run a chronic course of 2 yrs or longer. Once established, chronic episode lasts on an average 5-8 years[2].

DEMOGRAPHIC VARIABLES

Sex: Major Depressive Disorder is more common in women (1.5 to 2 times more)(2). Different explanations (such as artifactual and symmptmatological differences and comorbid anxiety disorders) have been put forward to explain these differences (21,22) but a recent study concluded that female preponderance remains unexplained by sociocultural factors, comorbid disorders or symptomatological differences (23).

Age: The evidence of age as a predictor of relapse is mixed, with some studies showing that younger age is associated with increased rates of recurrence (24) and others demonstrating that age more than 40 years at onset is associated with increased rate of recurrence(25).

Other demographic variables such as marital status and rural versus urban domicile have not been found to be consistent predictors in the above mentioned studies. Self-esteem support appeared to be the most important component of social support and is found to be inversely linked to depression severity over time.

CLINICAL VARIABLES

Clinical variable that consistently predicts increased rates of relapse is an increased number of prior episodes of major depression[26] though a few studies have failed to confirm this relation[27]. A recent study showed that the rate of recurrence was on an average 1.6 times greater for bipolar patients than for unipolar patients. Nevertheless, the effect of the number of episodes were greatest for unipolar patients and the rate of recurrence increased on an overage 15% with every episode for unipolar disorder and 9% with every episode for bipolar disorder[27].

The risk of developing multiple episodes have been linked with female gender, family history of depression, alcohol consumption, adverse life events and suicide attempts.

The time interval between onset of depression and institution of adequate antidepressant dosage and premorbid neuroticism were significantly related to the length of illness[28]. Low family income, parental overprotectiveness, and low level of mastery prolong recovery[29].

Seasonal Affective Disorder (SAD, winter type): is a recurrent depression type that is characterized by a seasonal pattern in onset (autumn or winter) and remission (following spring or summer) of the depressive episodes. SAD may shift into no seasonal recurrent depression[30,31,32] and thus the factors involved in the course of non-seasonal depression may underlie the outcome in SAD also.

"Double Depression":75% of all patients with dysthymic disorders report having experienced major depressive episode at some point of their lifetime[33]. Dysthymic disorder has greater comorbidity, higher rate of dysthymia in first-degree relatives and greater childhood adversities[34]. Also, patients with double depression tend to have an early onset of major depressive disorder and greater number of episodes than persons with non-chronic major depressive disorder[35].

RELATION TO LIFE EVENTS

For three decades it seemed to be a well-established fact that undesirable life events and stressful life situations trigger depression. However recent studies with depressed inpatients did not replicate this earlier finding[36,37].

Multivariate analysis indicated the cumulative effect of life events within two years of course is best predictor of BDI score at the end of two years. Since overall consistency of significant results was more pronounced in the subjective than in the objective evaluation of the life event, the results fit the best circular pathogenetic model in interaction between life events, their individual evaluation by the patient and depressive symptoms[38]. In dysthymic patients, major depressions were significantly associated with a new

life event in context of an ongoing chronic stressor[39].

COMORBIDITY

Several studies have examined comorbid substance abuse and affective disorders but relatively little has been determined about the effect of substance abuse in bipolar disorders[40]. An early onset and twice the percentage of suicide attempts have been associated with alcoholic bipolars than non alcoholic bipolars[41,42].

Recently more consideration is being given to the co morbidity of depressive disorders with anxiety disorders leading to search of newer antidepressants with anxiolytic properties such as venlafaxine. Anxiety symptoms are said to be more common in individuals who develop a chronic depression, and subjects with early onset of depression are more likely to suffer from anxiety disorders[26].

When patients with affective disorders are assessed with structured interviews, approximately 60% of adult patients and 35% of adolescents meet criteria for at least one *personality disorder*[43,44] though controversy abounds as to whether the enduring pattern of personality disorder defining behaviours represent a sub clinical manifestation of affective disorders. Borderline, histrionic and narcissistic personality disorders occur most frequently.

PREVENTIVE TREATMENT

PHARMACOLOGICAL THERAPIES

Bipolar Illness: The preventive treatment consists of prophylactic treatment with a ***mood stabilizer***. ***Recommendations*** differ as to when a patient should be considered a candidate for such a treatment. The American Psychiatric Association Expert Consensus Guidelines (1996) sate that, for patients with bipolar I disorder who have had two manic episodes, one severe manic episode or a family history of a bipolar disorder, long term or lifetime prophylaxis with mood stabilizer is indicated. Maintenance treatment is desirable for bipolar II patients who have disruptive hypomanic episodes, particularly if these were severe or occurred close together. In addition maintenance treatment with mood stabilizer for bipolar II patients who are receiving antidepressant therapy is mandatory if there is a previous history of an antidepressant treatment emergent switch. Other recommendations consider depressive episodes and the frequency of recurrence: Long term prophylaxis is endorsed only after 3 manic, hypomanic or depressive episodes, or two such episodes that are severe or occur within a 5 year period or in the context of a family history of the disorder. These guidelines are too conservative, especially if the illness is of early onset. Prophylaxis might be provided after a first severe or psychotic manic episode in juvenile patients(based on high probability of recurrences in such patients)[70].

Following the discovery of the efficacy of lithium salts in controlling "psychotic excitement" by Cade[45], many more studies firmly established the prophylactic efficacy of lithium in recurrent affective disorders[46,47] including studies from India[48,49,50]. The role of psychosocial variables (Stressors, life events, social support etc) in modulating the response to ***lithium prophylaxis*** has also been studied[51,52] and a recent study from India[48] concluded that social support and stressful life events are significant correlates of response to lithium. Recently some doubts have been cast over the prophylactic efficacy of lithium[53,54]. Other studies have shown that lithium is effective as a prophylactic drug for bipolar affective disorders in only a proportion of patients[55,56] and also the recommendation of indefinite life long treatment has been questioned by some authors in bipolar illness[57]. The identification of ***prodromal symptoms*** early in the course of an episode may be useful in intermittent use of lithium[58] and recurrences of affective disorder could be treated earlier and perhaps more effectively[59]. Predictors of lithium failure include increasing number of previous episodes[60,61], rapid cycling[62,63], mixed or dysphoric mania[64], presence of borderline personality disorder[55] and in patients with neuroticism[60].

It appears that even in lithium responders, sub clinical symptoms and problems persist which may or may not justify additional intervention, depending on the doctor's and patient's motivation to optimize and ***fine-tune*** the treatment[65]. The measures to be taken will range from counseling, social support[48], general medical advice, well being therapy[66], cognitive therapy, family or group therapy or modified version of interpersonal therapy[65]. Finally, a change of medicine may also be considered, particularly in patients with subjective or objective cognitive impairments[67].

A large number of open studies have demonstrated the efficacy of ***divalproex sodium*** in long-term treatment[68]. Divalproex sodium has been shown to have a more favourable side effect profile, making it a first line choice for maintenance therapy for many clinicians. In one comparative study, discontinuation of prophylactic treatment as a result of side effect was recorded in only 10% of patients taking divalproex sodium, while accounting for 25% of the lithium treated group[69]. Moreover, it seems that divalproex sodium exerts a protective effect against both manic and depressive recurrence as against lithium's questionable efficacy on preventing recurrence of depression[70]. Open systematic data indicate that divalproex sodium is particularly efficacious in rapid cycling patients[71].

The efficacy of carbamazepine for bipolar disorder is widely recognized[72] and it is particularly useful as a monotherapy for patients who are difficult to treat such as those resistant to lithium and those with mood incongruent

atures.

For patients not responding to a single agent, it may be necessary to combine two mood stabilizers. Lithium - carbamazepines and lithium-divalproex sodium are the commonly used ***combinations***. A recent study showed that subjects treated with combination of lithium and divalproex were significantly less likely to suffer a relapse or recurrence but were significantly more likely to suffer one moderate or severe adverse side effec[73]. More systematic studies are needed to document the efficacy of these combinations in the long-term treatment of bipolar disorder.

Typical antipsychotics are frequently used In the maintenance treatment of bipolar disorder[74,75,76] but there is no compelling data from controlled trials indicating that these agents are effective as maintenance treatments[77,78,79] and they may exacerbate or precipitate depressive symptoms.[77,80,81].

Preliminary data suggest that ***clozapine*** may have long term efficacy in preventing mood episodes[82,83,84] and recently in a one year long ,open-label extension trial, ***olanzapine*** was found to maintain improvement in manic symptoms in patients who responded in the acute phase placebo controlled trial[85].

To our knowledge, there are no long-term maintenance data to date regarding risperidone, quetiapine, or ziprasidone in patients with bipolar disorders.

Unipolar Illness: Regardless of how the level of response is defined, the persistence of residual symptoms after treatment is a sign of poor prognosis and predicts more probability of relapse and recurrences[86,87]. Thus rather than a short term response, a full remission and long term recovery should be the ***goal to treat depression***[88].

The role of ***tricyclic antidepressants*** in the long term treatment of depression has been a subject of research since the early sixties,, but most of these studies suffered from glaring drawbacks— small sample size, missing specification of the investigated phase and only very few long tem trials with amitryptiline, most being with imipramine. Most of these studies were in fact continuation phase trials[89]. A recent metanalysis by Dang and Engel[90], however strongly supports the recurrence preventive efficacy of cyclic antidepressants. On the other side relatively high non response rates[91], a problematic side effect profile and a presumed mania inductive potential make the role of tricyclic antidepressants in the prophylactic treatment of unipolar depression still controversial. Some studies have reported antidepressant withdrawal mania also[92]. Another study compared the relative efficacy of full dose or half the dose used in acute phase of imipramine and indicated that the reduced dose was not effective in maintenance phase[93].

Increasing evidence suggests the prophylactic efficacy of **lithium** in unipolar depression and according to metanalysis on placebo controlled studies, no differences between lithium and antidepressants can be claimed. One multicentre study[94], compared lithium and amitryptiline in a long-term treatment regimen over 3 years and indicated no difference between the two drugs.

Many continuation phase studies have been done on serotonin-specific reuptake inhibitors?(SSRIs) but very few maintenance phase trials have been reported[95,96,97] and all of these studies are optimistic about the use of these agents in preventive treatment of recurrent depression.

Other studies have shown the efficacy of venlafaxine[88], mirtazapine[98], and milnacipran[99] in preventing relapses and recurrences in one to two years follow ups.

Psychotic Depression:The available data indicate that the ***combination*** of a typical anti-psychotic and an anti-depressant is superior to either agent alone[100,101,102]. There are, however, no randomized, controlled trials of typical anti-psychotics in the treatment of psychotic depression published to date. Remarkably little is known about the optimal duration of anti-psychotic treatment in psychotic depression[103]. The available reports suggest that the risk of psychotic or depressive relapse may be high if typical anti-psychotics are discontinued before one year of remission[104,105].

COMPLIANCE ISSUES

Instead of compliance, it has been suggested that the term ***adherence*** be used which puts more of a burden on the clinician to form a therapeutic alliance with the patient which thereby increases behavioural compliance[106]. The cornerstones of increasing compliance or adherence include education of, information for, and active participation by the patient in treatment process such as ***information*** about the illness, medications and what to expect from the treatment and removing misconceptions (e.g. depression being a natural reaction or being incurable or medications being addictive or mind altering)[107]. ***Family members*** are also to be informed and educated and ***objective measures*** of compliance such as serum level measurements and written "home work" in psychotherapy are to be carried out[108].

The common use of three or more drugs and dementia pose particular risk of noncompliance (overuse, abuse, forgetting, alteration of doses and schedules) in the ***elderly*** and they should be given pill containers with easier accessibility, large print labeling, daily dosing pill boxes, simplified dosage schedules and a careful consideration about an interaction between over the counter medications and prescribed drugs as a cause of non-compliance [109].

Management of ***side effects*** is another important issue in maintaining compliance. ***Somnolence and insomnia*** are two common side effects. Ruling out residual psychiatric illness,"switches", comorbid medical illnesses (e.g. thyroid

problems), concomitant medications, and disruption of nocturnal sleep cycle are the first step. Then strategies such as adjusting dosage schedules or doses, using additional medications(e.g. trazodone, zolpidem and mirtazapine for insomnia and stimulants for somnolence) or switching the anti depressant to another one are to be considered[110].

If specifically queried, the prevalence of ***sexual dysfunction*** with antidepressants is 2-95% with TCAs, 4-75% with SSRIs, 3% with bupropion and less than 1% with nefazodone and mirtazapine. Management includes adjusting the doses, waiting for the adverse effects to fade away, drug holidays, adjunctive pharmacotherapy (e.g., cyproheptadine, methylphenidate, bupropion, mitazapine), switching antidepressants; the best strategy being to start with an antidepressant that has little or no sexual side effects (e.g. bupropion, nefazodone and mirtazapine) if possible[111].

Increased appetite or weight gain is another troublesome side effect and after ruling out other potential causes such as hypothyroidism, advices to increase physical activity, lower calorie intake, increase intake of fruits or fluids and "waiting to feel full" may help. Pharmacotherapy in the form of stimulants, H2 receptor blockers (e.g. famotidine) and topiramate (a new anticonvulsant for which preliminary data demonstrate mood stabilization in refractory mood disorders,and has been associated with weight reducing properties) is then to be considered[110].

As patients improve, it is important that they learn how to measure symptoms and side effects and in this regard self-report inventories (such as Beck Depression Inventory, and Caroll Rating Scale for Depression[112] are more accurate than clinician rated global reports.

A key issue in managing patients during maintenance therapy is the ***differential diagnosis of symptomatic worsening*** viz- non pathological spontaneous fluctuations (blips), precursors to the return of illness, substance abuse, general medical conditions, other medications, drug interactions, non adherence, change in psychiatric diagnosis and life events[115].

PSYCHOTHERAPIES

The recognition of prodromal symptoms and psycho-education of partners of bipolar manic patients to make them aware of the specific early symptoms has been proved to reduce the social impairments and financial losses[113,114].

Only a few studies have been done on psychotherapies in the maintenance phase in depression.Behaviour therapy (BT) may be as effective as cognitive therapy (CT) and interpersonal therapy (IPT) but the later 2 approaches have attracted considerably more attention of late.

A recent study suggested that the strategy of offering IPT to women with recurrent unipolar depression and, in the absence of remission, adding antidepressant pharmacotherapy can be a highly effective treatment especially to women in child bearing age as it avoids chronic maintenance medication exposure because of the high rates of remission with IPT alone[116]. Another study concluded that IPT alone or in combination (with placebo or imipramine) was an effective maintenance strategy[117].

The out patient CT studies available do not have sufficiently lon g follow-up periods to assess its prophylactic efficacy thou h a few studies have proven its efficacy in relapse prevention, alone or in combination with pharmacotherapy and suggest a trend for CT to be non significantly better than maintenance pharmacotherapy[118,119].

CONCLUSION

Considering the high prevalence of recurrent mood disorders, it was pertinent to review the vast amount of research that has been done to understand the natural history of these disorders & it seems that bipolar and unipolar recurrent affective disorders have quite distinct longitudinal courses in terms of age of onset, duration of episodes, relapses, recurrences, predictors and relation to life events which was discussed in depth in this review along with a brief review of the rapid cycling mood disorder, "double" depression, seasonal affective disorders and comorbid disorders. The natural history has a bearing on preventive treatment whether it be pharmacological treatment, psychotherapy or compliance issues. Today pharmacotherapy is the mainstay of preventive treatment in these disorders with special care to be given to compliance issues and an adequate understanding of the psychotherapies.

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GALL BLADDER POLYPS

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With improvement in ultrasound technology, an increasing number of polypoid lesions of gall bladder (PLGs) are being diagnosed. The patients with gall bladder polyps usually present with pain in the right hypochondrium similar to that of symptomatic gall stones. Rare presentations may be acalculous cholecystitis, haemobilia and obstructive jaundice because of dislodgment of the polyps.[1] The gall bladder polyps can be found in any age from third decade onwards but they are more commonly seen in 4th to 6th decades of life. Equal distribution of gall bladder polyps has been noticed in both sexes in most of the series.[2] However, some authors have reported either male or female preponderance in their series as well.[3,4]

The risk factors for gall bladder polyps are not same as far gall stones, though some Japanese series show obesity as a strong predisposing factor.[5] An inverse relationship with smoking has also been suggested.There is a wide range of pathological lesions which masquerade as gall bladder polyps. An ordered classification of PLGs has been provided by Christensen and Ishak.[2]

They have classified the gall bladder polyps into benign and malignant, the former being further sub classified into true and pseudotumours (Fig1).

The cholesterol polyps are the commonest form of gall bladder polyps forming over 60% of all resected lesions.[6] In our patients also, the cholesterol polyps (Fig2 & Fig3)constituted a major chunk of the cases. An associated chronic cholecystitis has been reported in a large number of patients with gall bladder polyps. Many authors have reported an adenoma- carcinoma sequence in the gall bladder polyps similar to the one occurring in colonic cancers.[7,8] No such evidence was seen in our cases. Cellular atypia and mild to severe dysplasia can be demonstrated in adenomas and there are reports of adenomas staining positive for oncofetal antigens such as Carcina embryonic antigen and alfa feto proteins.[9,10]

As far as diagnosis of the gall bladder polyps is concerned, ultrasonography has been reported to be sensitive in 40-90% of cases.[8] In most of the series,the benign and malignant tumors, have been reported with a similar frequency of 5-10%, thus making it difficult to differentiate the malignant and benign lesions on ultrasonography.[6] It is usually considered that lesions smaller than one cm. are benign in nature and lesions bigger than one cms in size are malignant.We have depended exclusively on ultrasonography in our patients.

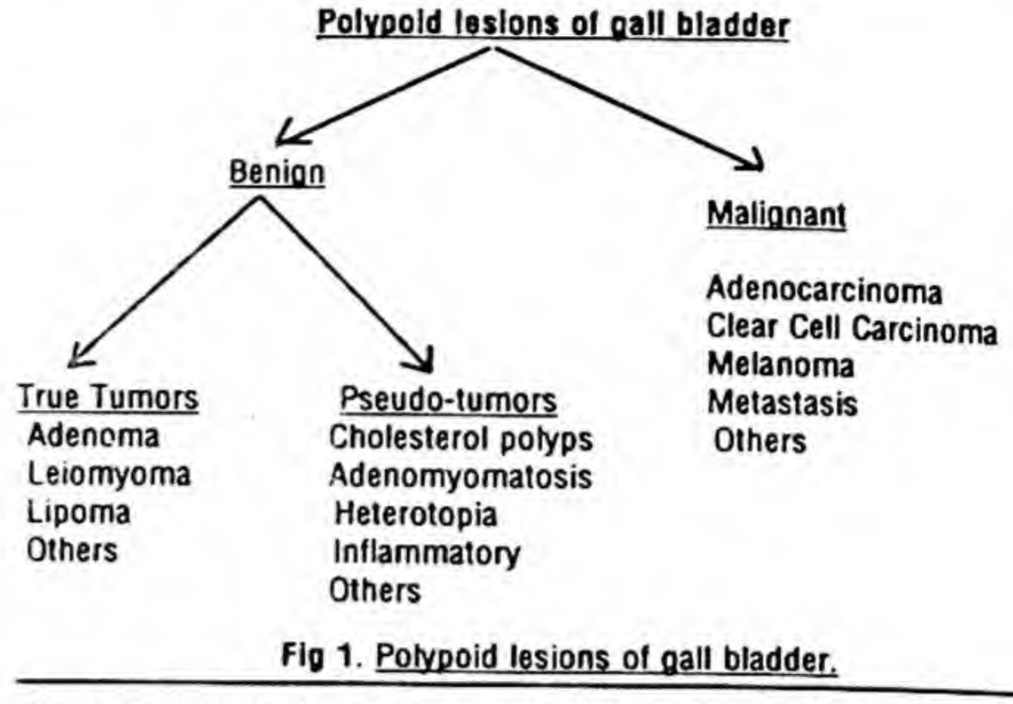

Fig 1. Polypoid lesions of gall bladder.

The oral cholecystography that has a sensitivity of only 20% was not used by us, nor were CT scan or ERCP done. There are reports that have suggested that transoesophageal and colour doppler ultrasound.[3,6] may aid in the preoperative diagnosis of gall bladder polyps. But these modalities are not widely available.

The factors that increase the chances of a gall bladder polyp being malignant include- age more than fifty years, presence of single polyp more than one cm in size, presence of gall stones in a sessile lesion even of less than one cm in size and rapid enlargement in the size of a polyp on serial ultrasonography.[6,11,12] There are number of reports suggesting that sessile lesions less than one cm in size have an increased incidence of malignancy as compared with those having a stalk.[10]

The correct surgical management of gall bladder polyps is controversial. It is widely agreed upon that all the sympatomatic gallbladder polyps should be offered a cholecystectomy, preferably a laprascopic cholecystectomy.[12,13] But what should be done for the patients who are asympatomatic? For example there are a couple of such patients with us under observation. A young male who was operated for hernia and underwent pre-operative ultrasonography of abdomen was diagnosed as having GB polyps measuring from 3mm to 4mm(fig 5). He refused surgery and has been undergoing periodic ultrasonography to monitor the GB polyps. Another patient,

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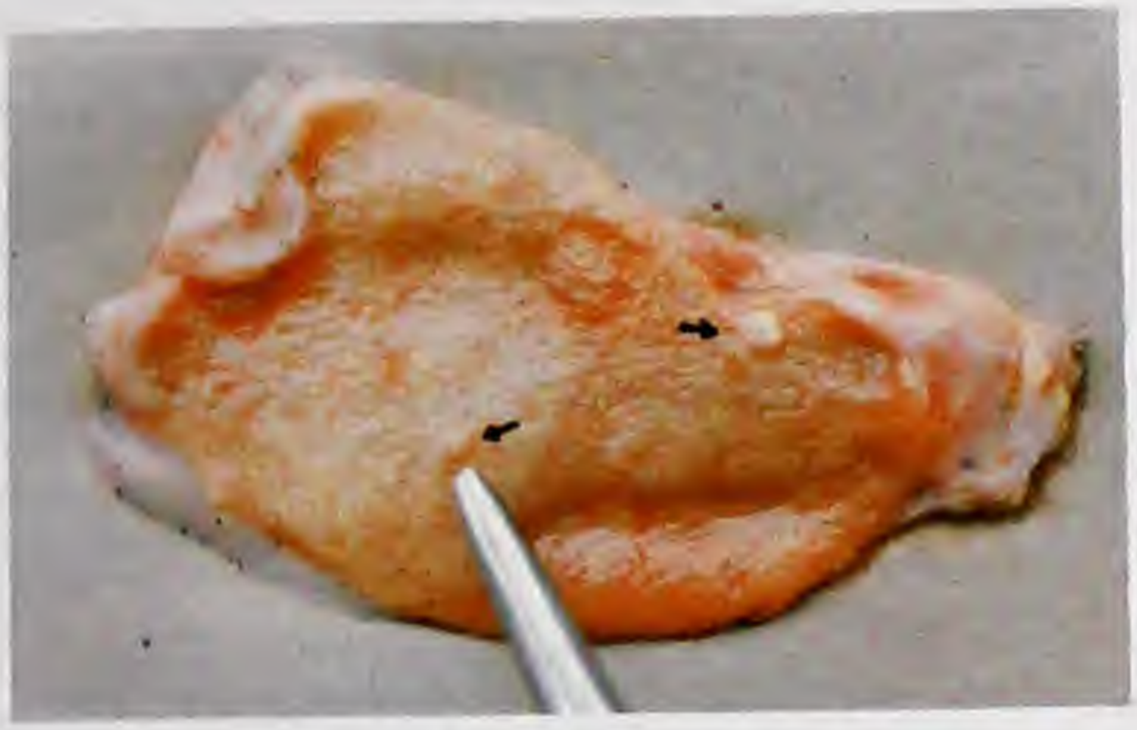


Fig-2: Photograph of resected gallbladder showing two cholesterol polyps (arrows)

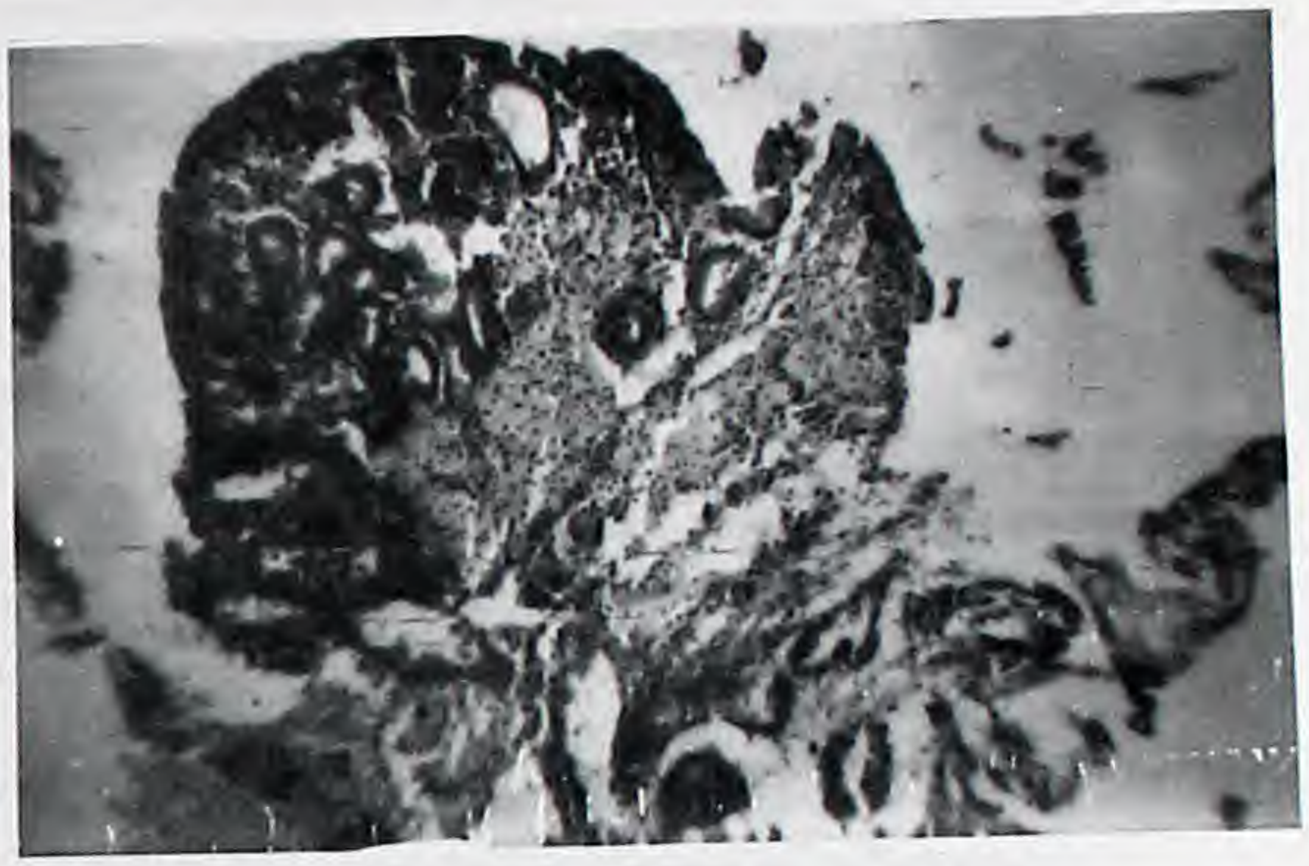


Fig-3: Photomicrograph showing a cholesterol Polyp in a resected gall bladder (x100)

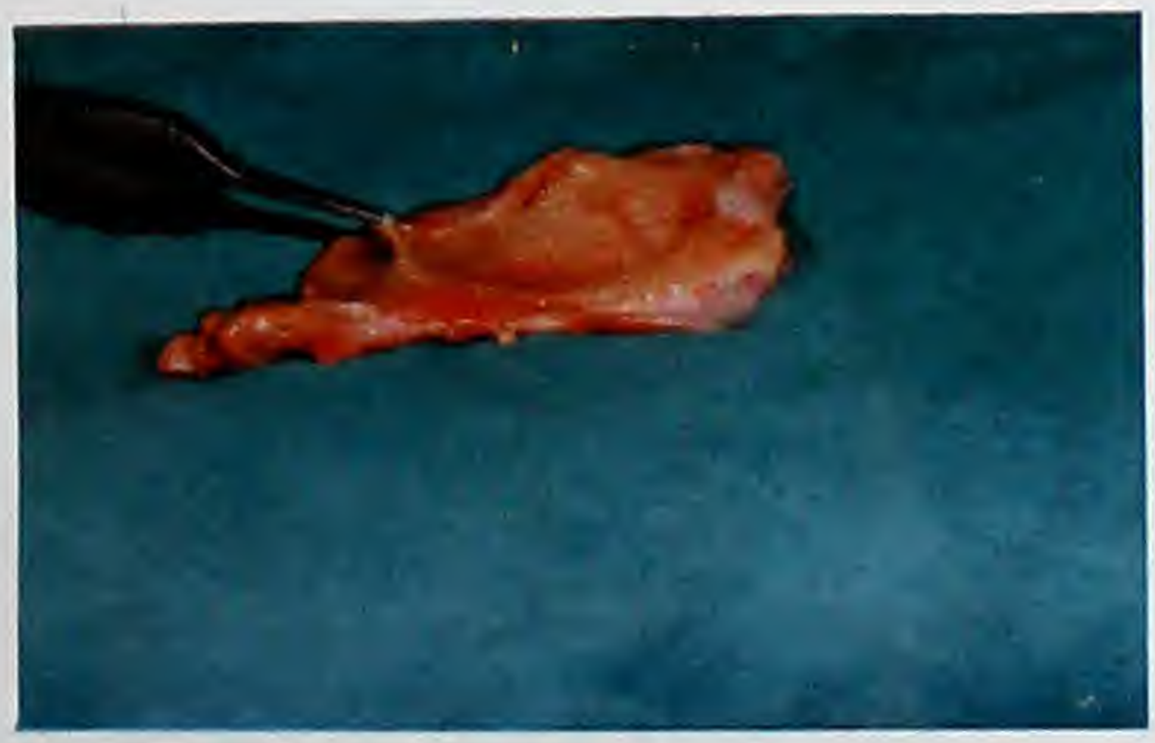


Fig-4: Photograph showing a Pendunculated Polyp in an opened up gall bladder.

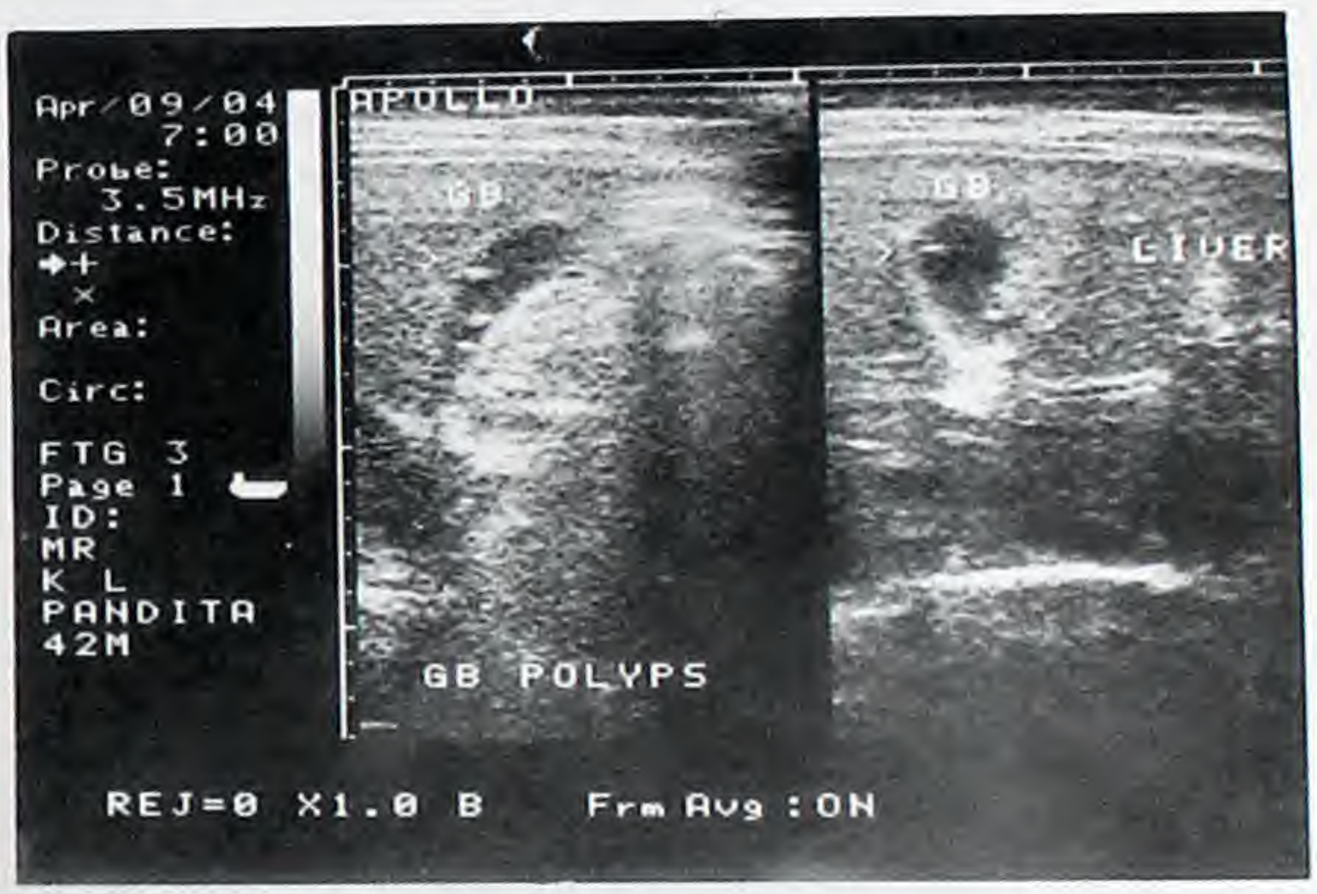
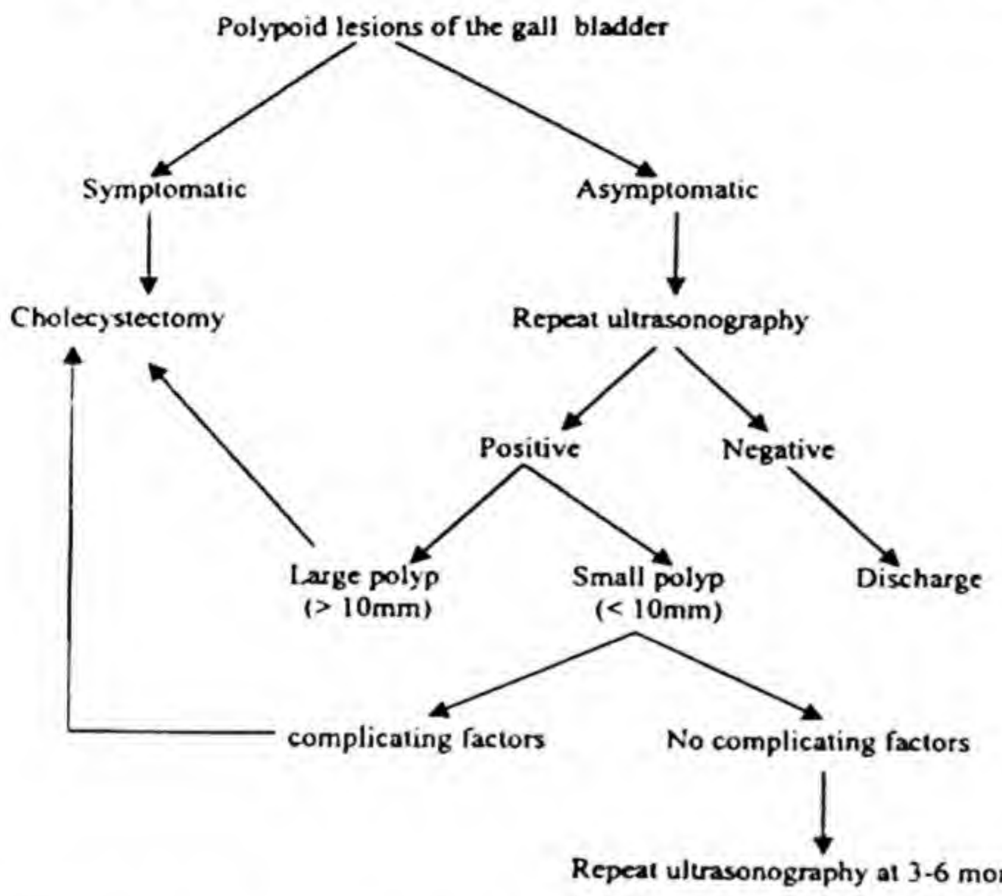


Fig-5: Ultrasonographic image showing sessile gall bladder polyps.

a middle aged female with gastroesophageal reflux disease (GERD), who was advised routine USG abdomen, was found to harbour a 5mm sessile fundal polyp in the gall bladder, but refused surgery and strongly contends the treatment vis-à-vis relief of her symptoms. For large polyps with a greater chance of malignancy, traditionally the patients should undergo open cholecystectomy so that in case more extensive procedure, if needed, can be done. However, there are other authors, who have proposed that laproscopic cholecystectomy using a retrieval bag to prevent port-site implantation appears to be sufficient for malignant lesions that have not breached the gall bladder serosa.[13] In a study of 34 patients by Mainprize et al, it was not possible to predict the nature of gall bladder polyps before operation and a high incidence of neoplasms, both benign and malignant (4 cases) in young patients worried them.[14] In our patients, which is no doubt a smaller series (21 cases), none of the patients had any evidence of malignant lesions.Some other series have reported false positive scans and postulated that the reasons for this were presence of polypoid cholecystitis at the time of scan,

Fig:6: Management protocol for GB polyps - (Modified)



mistaking gall stones as polyps.Taking into account these inaccuracies of ultrasonography for diagnosing gall bladder polyps, the management protocol proposed by Boulton and Adams[15] has been further modified by Mainprize et al.

This scheme of management of polypoid lesions seems to be logical as all patients with symptomatic gall bladder polyp/s are offered laparoscopic cholecystectomy. As the sensitivity of the USG is variable, the asympatomatic patients are rescanned and are offered laparoscopic cholecystectomy if polyp is identified on second USG. If repeat USG doesn't show polyp s, further scan is performed after 6 months and patient is discharged if no polyp is seen now. Patients refusing surgery are followed with 6 monthly USG and if lesions increase in size they are once again offered surgery.

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NEWER ANTI ANGINAL & ANTI ISCHEMIC DRUGS

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Introduction:

Despite a large number of pharmacologic agents available for the treatment of ischemic & other cardiovascular diseases, extensive research for additional & more effective drugs & pharmacotherapeutic approaches continues. In this article some new drugs already in practice & some still investigational therapeutic agents are reviewed.

There are around ten new classes of drugs being evaluated in patients with angina pectoris & myocardial ischemia. They are as under;

1. First group includes *Potassium Channel Openers*. Various organs including myocardium & blood vessel: contain potassium adenosine triphosphate channels (KATP) in their cell membranes. During an episode of myocardial ischemia, there is a reduction in intracellular myocardial ATP leading to the opening of KATP channels. This result in an efflux of intracellular potassium, hyperpolarization of the cell membrane, shortening of action potential duration & both myocardial & vascular relaxation. The potassium efflux that occurs during ischemia has been shown to be protective & thus prevents further myocardial damage, thereby preserving myocardial function - *ischemic preconditioning* Currently large scale trials are in progress assessing the antianginal efficacy & safety profile of these drugs. Nicorandil is a coronary & peripheral vasodilator that has a complex mechanism of action & appears to have a short duration of action, requiring frequent dosing[1]. Its potential advantages is that unlike nitrates it is not associated with any tolerance. Other orally active ATP potassium channel openers which have been used in treating angina include Cromakalin & Pinacidil[2].
2. Second group includes *Nitric Oxide Donors*. Nitric oxide has been shown to be an important biological substance involved in normal physiologic functioning secreted by normal endothelium. It is an endogenous vasodiaitor. Endothelial cell dysfunction often leads to diminished nitric oxide production which may be an etiologic factor in atherosclerotic vascular diseases. The various drugs in this group are from Sydnonimine class[3] & includes Molsidomine, Persidomine & CS-780. The drugs are not associated with pharmacologic tolerance & ongoing clinical trials using these compounds in angina pectioris are now in progress. Recent data suggest that long term nitrate therapy may be deleterious in the treatment of angina pectoris[4,5].
3. Third group of newer anti anginal are *Sinus Node Inhibitors*. These drugs reduce heart rate a by non-B receptor mediated mechanism & have no direct negative ionotropic effects. The prototype agent includes Zatebradine. It decreases the rate of spontaneous depolarization of pacemaker cells in the S.A. node thus producing sinus node inhibition[6]. Zatebradine has no effect on calcium channels & it has no effect on the peripheral vasculature of the myocardium. The drug can antagonize an Isoproteranol mediated increase in heart rate in a non-competitive fashion without affecting contractility. However, preliminary findings suggest that Zatebradine may not be effective in angina despite their heart rate lowering effects[7]. Tedisamil, another sinus node inhibitors is now being evaluated in clinical trials.
4. The fourth class of agent include *pFOX Inhibitors* which act as partial inhibitors of myocardial fatty acid oxidation & include Ranolazine & Trimetazidine. Ranolazine is without haemodynamic effects, however, it appears to improve myocardial ischemia by shifting ATP production away from fatty acid oxidation toward carbohydrate oxidation[8]. The drug has been evaluated in patients with angina showing some benefit[9].

Trimetazidine demonstrates a number of potentially useful cytoprotective actions that include a limitations of mitochondrial & membrane damage caused by oxygen free radicals[10], a reduction of intracellular acidosis & an inhibition of neutrophil infiltration in the perfused myocardium[11].

In multiple clinical studies Trimetazidine has demonstrated significant anti ischemic actions. In patients with chronic stable angina, Trimetazidine has reduced anginal attack frequency & nitroglycerine consumption, while increasing treadmill exercise time & the time to development of 1 mm segment depression on exercise ECG. The drug is as effective as Propranolol & Nifidipine on both angina & exercise parameters & can provide additional benefit when added to Diltiazem, Nifidipine or blockers. Trimetazidine was also shown to improve the coronary micro circulation & reduce the number of ischemic episodes in patients with angina pectoris who underwent ambulatory ECG monitoring[12].

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5. The fifth group of agents include *Complement Inhibitors.* In experimental studies complement inhibition appears to optimize recovery during the revascularization of ischemic myocardium[13]. Clinical trials have started to investigate this pharmacologic treatment.
6. The sixth class of drugs include *Aldose Reductase Inhibitors*. These drugs are shown to preserve the tissue redox ratio of nicotinamide-adenine dinucleotide to reduced form of NAD (NAD/NADH)[14] which can be protective in myocardial ischemia. In experimental isolated heart studies in diabetic rats, aldose reductase inhibitor zopolrestate preserved ATP during global ischemia, reduced ischemic injury as measured by CPK release & improved functional recovery of myocardium after reperfusion[14]. In addition Na+ / K+ ATP activity increased limiting the rise of intracellular sodium & hence intracellular calcium rise during ischemia & reperfusion. Clinical trials with Zopolrestat in diabetic & non-diabetic patients with angina pectoris are in progress.
7. The seventh class of anti ischemic agents are *inhibitors of Sodium-hydrogen ion exchanger (NHE)*. This exchanger pumps the sodium into the cell which is in turn exchanged with calcium thus increasing the intracellular levels of Ca++. The exchanger is markedly active in ischemia & reperfusion. inhibition of this exchanger definitely decreases intracellular Na+ & subsequently decreases intracellular Ca++ overload. Inhibitors also decrease the rate of ATP depletion during ischemia & reperfusion> Such action reduces the chances of malignant arrhythmias as well as the development of myocardial necrosis[15]. Amiloride & analogues have been proved to be potent NHE inhibitors. However, amiloride alone is non-specific & must be taken at excessively high levels to be effective which can prove to be toxic. In contrast another analogue such as cariporide which has undergone clinical investigation has been seen to be more potent & more selective, accomplishing the same desired results of NHE inhibition, while not requiring excessive doses for effectiveness. Therefore analogues are preferred as potential treatment for clinical use to prevent reperfusion injury.

   The most promising situation for NHE inhibitor use is a typical ischemia reperfusion situation when the inhibitor can be present at all times, such as during cardiac surgery. It could also be beneficial in cardiac transplantation & PTCR where coronary blood flow is transiently stopped. Use of these inhibitors also may be effective in patients with unstable angina pectoris & myocardial infarction when there is risk of contractile abnormalities & arrhythmias.
8. The eight class of drugs include the *Statins* (Lovastatin, Simvastatin, etc.) & *Acyl-COA cholesterol acyl transferase inhibitors (e.g. Avasimibe)* which appear to improve endothelial cell functioning & vascular reactivity independent of cholesterol lowering effects[16]. These drugs are now being evaluated as anti anginal drugs. A trial has begun which is designed to study the effects of pravastation on high sensitivity C-reactive protein plasma levels, a specific marker for active inflammation in patients with coronry artery disease & possible cause of myocardial ischemia & atherosclerotic plaque instability.
9. The ninth class of agents include *Insulin Senstizing drugs* that appear to improve endothelial function. Troglitazone has been shown to be useful in the treatment of vasospastic angina[17].
10. The tenth of agents are biological substances called *angiogenesis agents*[18]. Angiogenesis means the formation of new capillaries form pre existing blood vessels. The process includes the degradation of basement membrane of endothelial cells in response to cytokines followed by migration of endothelial cells in response to cytokines followed by migration of endothelial cells from the parent blood vessel in a directional manner towards the stimulus, invading the extravascular space; endothelial cells proliferate & migrate through the connective tissue to a target site where they assemble to form a new vessel & lumen & secrete basement membrane.

    Angiogenesis agents include:

    - *Extracellular matrix molecules*, like fibronection, fibrine, collagen, laminin.
    - *Growth factors & cytokines*, like FGF (fibroblas growth factor)
        - Vascular endothelial growth factor (VEGF).
        - Platelet derived growth factor (PDGF).
        - Epidermal growth factor (EGF).
        - Hepatocyte growth factor (HGF).
        - Tumor necrosis factor - alpha (TNF- alpha).
        - Protaglandin E2 (PGE2).
        - Transforming growth factor-beta (TGF-beta).
    - *Hormones like*
        - Granulocyte macrophage colony stimulating factor (GM-CSF).
        - Estrogen & Progesterone.

    Some of these factors are being used in clinical trials to treat pateitns with coronary artery disease & angina pectoris.

    Vascular endothelial growth factor (VEGE) is a secreted homodimeric glycoprotein with 4 different isoforms generated from an alteration splicing mechanism in humans. VEGF binds to specific cell receptors flk.1 & flk.1. The biological activity of VEGF-165 has been studied most extensively because it is the

predominant isoform secreted by a vriety of cells. VEGF-165 & VEGF-121 are being studied in clinical trials of patients with severe angina pectors, being injected directly into either the coronary or peripheral circulation. In other studies naked DNA containing VEGF gene was injected directly into sites in the myocardium identified by angiography. Access was obtained by minithoracotomy. Other investigators injected the VEGF gene into cardiac muscle aboard a disarmed adenovirus vector during coronary artery bypass surgery or during minithoracotomy. Some short term preliminary studies have revealed clinical benefit in patients with severe angina pectoris, with evidence of increased blood flow to the heart. In some studies the resutls have been unimpressive[19].

Another angiogenesis substance under investigation has been fibroblast growth factor (FGF). The FGF gene presently contains 9 members. FGF-1 (acidic) & FGF-2 (basic) are single chain polypeptides. these molecules promote formation of new blood vessels & the proliferation of vascular smooth muscle cells. FGF-1 & FGF-2 have been administered to human beings with angina pectoris & severe coronary artery disease by direct intracoronary injection & by direct intramyocardial injection. Intramyocardial delivery of naked DNA containing the FGF gene & delivery of the FGF gene by adenovirus have also been used. FGF-2 has been implanted in pellet form in the myocardium in patients undergoing incomplete coronary revascularization procedures[20]. Early results with FGF have been favourable but more long term data are needed.

Other angiogenesis stimulatory substances under investigation ar/e hepatocyte growth factor & hypoxia inducible growth factor. Inflammatory mediators of angiogenesis are also being investigated as potential clinical agents.

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ORIGINAL ARTICLE

JK-PRACTITIONER

EVOLUTION OF SYMPTOMS IN CHILDHOOD AND ADOLESCENT MANIA

Subhas Chandra Gupta, DPM.; Soumya Basu, DPM.; Vinod Kumar Sinha DPM, MD.

Abstract: *Pattern of evolution and appearance of prodromal symptoms has been of importance in clinical medicine for many progressive, and treatable diseases but except for schizophrenia, research on evolution and prodromal symptoms in psychiatry has been largely anecdotal. Thus, this study was conducted to find the average duration of evolution and prodrome in childhood and adolescent mania, its symptoms and to assess the difference in duration of evolution and prodromes on the basis of sex, mood and age. 30 consecutive patients of age 19 years or below, fulfilling the Diagnostic Criteria for Research, ICD-10 for manic episode or bipolar affective disorder, manic type were taken up for the study. A checklist was then applied for symptoms of mania as well as associated other symptoms. The mean duration of evolution was 42.2 days .Twenty-two out of the 30 patients (73%) had a prodrome with a mean of 20.3 days. A significantly longer prodromal period was found in age group of 12-16 yrs. (Mean 22.9 days) than in age group of 17-19 years (Mean of 7.9 days). Decreased sleep and increased self-esteem were the most common prodromal symptoms.*

Key words- *Evolution, Prodrome, Mania, Childhood , Adolescent.*

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INTRODUCTION:

The history of mania in children and adolescents extends back at least to Kraepelin[1] who recognised that the condition occurs in about 0.4% of his patients by age 10 years, 3% of his patients by age 15 years and 20% by age of twenty. Patric G. Coll et al.[2] attempted to confirm the occurence of manic depressive illness in childhood and adolescents which was at that time thought to be uncommon.

Geller et al.[3] after reviewing extensive literature reported that mania had been previously under diagnosed and misdiagnosed in children and adolescents.

As yet, no national or international epidemiological study of bipolar disorder during the pediatric years is available. However,studies[4,5] have suggested that prevalence during the adolescent years is at least that of the adult population.

Recent studies[6,7] have concentrated on identifying symptoms of mania early in the evolution of episodes. Social workers have been engaged to detect early relapses[8] and refer such patients to minimize the undesirable consequences like ruined carriers, financial losses, illegitimate pregnancies, and unnecessary restraint[9]. Except for schizophrenia, research on prodromal symptoms in psychiatry has been largely anecdotal[10-14]

The recognition of prodromal symptoms is already gaining much importance as is highlighted by psycho-educational programmes for partners of bipolar manic patients[15]. The NIMH working parties[16] and Scott[17] highlighted the need for research and development of methods for psychological intervention in bipolar affective disorder, one obvious candidate being early intervention during prodromes.

In addition, the recommendation of indefinite, life long treatment has been questioned by some authors[18] in bipolar illness. Therefore, identification of prodromal symptoms early in the course of illness may be useful in intermittent use of lithium[8] and recurrences of affective disorder could be treated earlier and perhaps more effectively [6].

MATERIALS AND METHODS:

The present study was conducted at Central Institute of Psychiatry (C.I.P.), Ranchi. It is a post graduate teaching hospital, which has got a wide catchment area which includes the states of Bihar, Uttar-Pradesh, West-Bengal, Himachal Pradesh, Orissa and some parts of Madhya Pradesh and North Eastern states and also from neighbouring countries like Nepal, Bhutan and Bangladesh. It has a 15-bedded child psychiatry unit.

Selection of subjects: The present study had a prospective design and purposive sampling was done. 30 consecutive patients of age 19 years or below, fulfilling the Diagnostic Criteria for Research, ICD-10 (WHO, 1993) for manic episode or bipolar affective disorder, manic type were taken up for the study, after obtaining informed consent from the key relative to participate in the study.

Exclusion Criteria were-duration of episode greater than

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6 months (as subjective recall may be doubtful beyond that period), failure to get informed consent, accompanying guardian (key relative) not staying with the patient for the index episode and diagnosis of Organic Mania or Substance Induced Mania.

Assessment:

The key person / relative accompanying the patient fulfilling the above mentioned criteria was identified and informed of the purpose of study and an informed consent was taken. All patients taken up for the study were interviewed within 48 hours of their first contact in Out Patients Department and the severity of the index episode was then rated on Young's Mania Rating Scale (YMRS)[19]. Relevant information such as demographic and socioeconomic details, past history and family history of mental illness and personal history were recorded. The **symptom checklist**(available from corresponding author) was given to the key relative and was asked to tick the symptoms present. Later, relatives were asked to sequence the events in order of onset and date the individual symptoms as accurately as possible in the symptom check list. This is a self-generated checklist for symptoms to elicit and explore for the diagnostic criteria of manic episode and other associated symptoms. The duration between the first symptom uptil the day at which criteria for manic episode were fulfilled was taken as the prodrome while the difference in days between the appearance of first symptom and the last symptom was taken as the period of evolution. The drug treatment or any other modality of treatment was not controlled in the study.

Results:

Sample consisted of thirty patients -23 males and 7 females. 14 patients were in the age range 12-16 years and 16 patients in the age range17-19 years. The mean duration of evolution of the entire sample was 42.2 days with a maximum of 161 days and a minimum of 1 day. There was no significant difference in the period of evolution on the basis of age, sex or mood(euphoric vs. irritable)

The mean duration of prodrome for the entire samples was 14.9 days (SD+ 18.3). Twenty-two out of the 30 patients (73%) had a prodrome with a mean of 20.3 days (SD + 18.6). The minimum prodromal period was 3 days, and maximum 65 days.

A significantly longer prodromal period was found in age group of 12-16 yrs. (Mean 22.9 days; S.D + 21.0 days) than in age group of 17-19 years (Mean of 7.9 days; S.D + 12.3 days)**[Table 1]**

Out of the 30 patients, 22 had a predominantly irritable mood (73%) and eight had a predominantly elevated mood (27%). A significant gender difference was found when Chi-Square test was applied (Likelihood ratio = 0.02). All seven females had predominantly irritable mood whereas 15 out of 23 (65%) males had irritable mood.

Table1: Prodromal period in different sub-groups of the entire population(N=30)

Grouping criteria	Categories	Mean prodromal period (days)	S.D.(days)	Significance at .05 Levels
All	N=30	14.9	18.3	-
Age	12-16 yrs. (N= 14)	22.9	21.0	
	17-19 yrs. (N = 16)	7.9	12.3	p =.021
Sex	Male (N=23)	12.7	16.0	N.S.
	Female (N =7)	22.0	24.2	
Past history	Absent (N = 21)	17.9	19.1	N.S
	Present (N = 9)	7.9	14.8	
Predomi--nant mood	Elevated (N = 8)	21.4	21.6	N.S
	Irritable (N=22)	12.5	16.8	
YMRS	26-36 (N=19)	17.4	20.4	N.S
	37-46 (N = 11)	10.5	13.7	

NS = Not significant

If we consider the first three symptoms occurring in prodrome together, decreased sleep is the most frequent (45% of population) followed by big talks (41% of population) and increased self esteem (32% of population).

DISCUSSION AND CONCLUSION

The most targeted area of this study was the durations and patterns of evolution and of prodromal symptoms in childhood and adolescent mania. Acute or abrupt onset have been described[1,20] but the exact durations had remained elusive till Bunney et al[21] gave a time frame of 1-10 days and Molnar et al[6], a yet more precise duration of 21.14 + 22. 24 days; though Smith and Tarrier[22] also concluded that prodromal symptoms might precede the full syndrome by weeks; and Sclare and Creed[23] gave the time between the appearance of the first symptom of mania and admission to be varying from 2 days to over 4 months (Median 22 days).

This study shows a meanperiod of evolution of 42.2 days and prodromal phase of 20.3 days (SD = 18.6) with a minimum and maximum of 3 days and 65 days respectively. Seventy three percent of the population reported prodromal symptoms akin to 75% reported by Smith and Tarrier[22] but less than that reported by Keitner et al[7] i.e 93% .

In this study, within the sample, prodrome was significantly longer (Mean = 22.9 days) in younger age group (12-16 year) when compared with the 17-19 years age group (Mean = 7.9 days)[**Table1**]. A longer mean prodrome was found in females and patients with elevated mood, when compared to males and patients with

predominantly irritable mood (though none of these were statistically significant).

As shown in earlier studies[24], a significant proportion (73%) of patients had predominantly irritable mood and only 8 out of 30 (27%) had elevated mood. A significantly high prevalence of irritable mania in females (7 out of 7) as compared to males (15 out of 23) was also found.

Jacobson[8], while describing the *telltale sign* stressed the fact that each individual may have different symptoms thus emphasizing the heterogeneity of symptoms in a prodromal phase.

However, later studies[7,18,20-22,25,26] found certain symptoms which were consistent in all patients. These were symptoms like decreased sleep, increased activity, increased socialization, elevated mood etc. Wehr et al[27]hypothesized sleep disturbance to be the final common pathway leading to a manic episode.

In this study, decreased sleep was the most common first symptom occurring in prodrome (27% of sample who had a prodrome) followed by big talks (23% of population). Increased self-esteem was quite frequent amongst the most common first three symptoms (32%). An interesting clinical feature of many manic patients in this study was the ease at which they complied with the request to sing a song. Singing was thus assessed as a prodromal symptom and was found in 36% of population when the most common first five symptoms were considered together. Interestingly, elevated / irritable mood never predominated the prodrome though the acumen needed to detect this might be questionable in the patient's relatives in this socio cultural background.

Some limitations of this study are in the form of small sample size, non standardized symptom check list, no controls for drug treatment or any other form of treatment and no subject of less than 12 years of age. Again, unless prodromes are similar in duration and pattern across episodes, it would be difficult for the family or treating personnel to draw conclusions or generalize, hence the need to compare the initial date with that in follow ups and readmissions, thus requiring a prospective detection of manic prodromes rather than the retrospective approach used in this study.

The **strength and uniqueness** of the study lies in the fact that prodrome was demarcated when DCR-ICD-10 criteria for manic episode were fulfilled, thus making it more objective and definite rather than arbitrary and subjective to the discretion of the patient or the informant. With the present set of findings, patients and their family members can now be sensitized to early warning symptoms so that treatment can be initiated early to prevent a full blown manic episode and/or hospitalization.

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A STUDY OF END STAGE RENAL DISEASE PATIENTS FROM SOUTHERN PART OF ARABIAN PENINSULA.

(Aetiology of and Hepatitis B & C prevalence in Patients on Maintenance Haemodialysis)

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Abstract: *All the patients currently registered in the artificial kidney unit of Najran General Hospital were studied for the pattern of underlying disease and prevalence of Anti-HCV and HbsAg positivity. All patients positive for Anti-HCV were confirmed by immunoblot assay. Our patient showed a uniform distribution in all age groups with a slight peak in age group 30-39 in males (peak productive age). Diabetic nephropathy was the commonest identifiable cause of end stage renal disease in male. 45% of our patients had no identifiable underlying disease. In view of an evolving trend tof diabetes mellitus, diabetic nephropathy may become more important cause of renal failure in future. 46.2% of our patients were positive for anti-HCV antibodies and 10.4% were HbsAg psotive. Anti-HCV positivity was significantly more in patients above the age of 50 years, and those with a longer duration on hemodialysis. There was no significant relation with the number of blood transfusion received. We believe that spread of hepatitis C is nosocomial rather than transfusion related and more studies are needed to know the exact mode of spread in hemodialysis patients. Strict universal infection control precautions and proper disinfection procedures should be follc wed.*

Key words: *Hemodialysis, Anti-HCV, HbsAg, diabetic Nephropathy, and Najran.*

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Introduction

With the availability of haemodialysis, patients with end-stage renal disease (ESRD) are living longer than ever. Many of the patients are enjoying if not the normal but a reasonable quality of health. In view of the high prevalence of Diabetes[1] and Hypertenstion[2] in Saudi population, the magnitude of ESRD might reach epidemic proportions in future. It has been noted for some time that liver disease is common in dialysis patients. With the advent of kits for testing antibody against hepatitis C, it was also realized that Hepatitis C is more common in this subset of population.[3] We decided to go through the study of these patients in order to know the pattern of ESRD and prevalence of anti-HCV and HbsAg in these patients now so that it will serve as the baseline for a future reference. It will also help to complete the national level data in this country. To our best knowledge, there has been no such study so far from this south western province of Saudi Arabia called Najran.

Material and Methods

This study was conducted on all the registered patients of artificial kidney unit (AKU) of Najran General Hospital in the month of Rabi-II 1421 (June 2000). This is the only Ministry of Health (MOH) hospital with this facility in Najran in addition to a very small setup in the town of Sharorah. Patients from all over the region are referred here. All patients with renal failure are followed here and put on maintenance haemodialysis when needed. Non-Saudi patients are not dialysed except by special permission or incase of an emergency. We analysed the data collected from all our patients. Data was collected under following headings. Name, age, sex, nationality, duration on dialysis, blood transfusions received in last three years, hepatitis B surface antigen (HbsAg), antibody against hepatitis C (Anti-HCV) in addition to all routine investigations. HbsAg was performed using Auszyme Monoclonal by Abbot Laboratories and confirmed by neutralization method Anti-HCV was done using Murex Anti-HCV (version 4.0) by Abbot murex Laboratories. positive cases were confirmed by immunoblot test using Chiron "RIBA" HCV 3.0 SIA which is supposed to have a specificity of 98.8%. Standard statistical methods were used for calculating mean, standard deviation (S,D) and significance value (p).

Results

We studied a total of 67 patients, currently registered in our unit and getting regular haemodialysis. it comprised of

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37 males and 30 females (male, female ratio of 1.2:1). There were 29 Saudi males and 24 Saudi females. 14 non Saudis were mainly Yemenis except two Palestinians who were on dialysis for less than six months. Age ranged from 13-66 years (mean 39±12.8 years) in males and 15-62 years (mean 38.51±11 years) in females. Age distribution with HbsAg posivity and Anti-HCV positivity is given in Table 1 and Table 2 shows the underlying cause of ESRD. Table 3 shows a detailed distribution of HbsAg and anti-HCV patients and Table 4 shows the relation of Anti-HCV positivity with three variables namely duration on hemodialysis, number of blood transfusions received in past three years and age above 50 years.

Table-1: Showing distribution of patients in relation to age and HbsAg and Anti-HCV positivity

Age In Years	Total	Males (M)	Females (F)	Anti-HCV positive M+F	HbsAg positive
<19	7	3	4	0+2=2	1
20-29	10	6	4	3+1=4	1
30-39	16	10	6	6+2=8	2
40-49	8	4	4	1+1=2	3
50-59	13	6	7	3+4=7	none
>60	13	8	5	5+3=8	1
Total (%)	67(100)	37(55.22)	30(44.77)	31(46.2)	7(10.4)

Table-2: Showing underlying cause of ESRD

Disease entity	Males	Females	Total (%)
Diabetic nephropathy	10	3	13(19.4)
Glomerulonephritis	2	1	3(4.49)
Pyelo nephritis	2	5	7(10.44)
Polycystic kidney disease	2	2	4(5.9)
Collagen vascular disease	nil	3	3(4.49)
Obstructive uropathy	2	1	3(4.49)
Alpports syndrome	4	none	4(5.9)
Not established	15	15	30(44.77)
Total	37	30	67(100)

Table-3: Showing distribution of HbsAg and Anti-HCV positive patients in relation to nationality and gender.

Nationality	Gender	Total	HbsAg positive	Anti-HCV positive	Positive HbsAg and Anti-HCV	Negative HbsAg and anti-HCV
Saudi	males	29	5	14	none	10
Saudi	females	24	0	9	none	15
Non-Saudi	males	8	2	6	1	1
Non-Saudi	females	6	0	2	none	4
Total (%)		67(100)	7(10.44)	31(46.26)	1(1.49)	30 (44.77)

Table-4: Showing relation of Anti-HCV status to three different variables

Variable	Anti-HCV positive Patients (n=31)	Anti-HCV negative patients (n=36)	Significance (p value)
Mean duration on haemodialysis ± S.D. (in months)	46±12	21±9	p<0.001 Significant
Number of transfu--sions received in last thee years	0.3 per patient	0.4 per patient	p>0.05 non-significant
Age above 50 years versus below 50 years	15:16	11:25	P<0.001 Significant

Discussion:

ESRD is one of the devastating disease and causes severe emotional psychological and physical dysfunction to the patient and a considerable economic burden on the state. According to an estimate it costs 75,000 to 100,000 Saudi Riyals to provide haemodialysis to one patient for one year. Although haemodialysis is provided free of charges to all Saudi nationals. In view of an evolving epidemic of diabetes, the magnitude of this disease might increase very rapidly in future. In our study we have mainly Saudi patients (53/67). Our of the non-Saudi patients the majority were Yemenis (12/14). Yemen is the neighboring country and the population does not differ in culture, traditions and possibly in genetic makeup. So we believe that this sample should be considered representative of the entire geographical zone rather than Najran province alone. Male, female ratio of 1.2:1 was found and ESRD patients showed a uniform distribution along the age scale with a slight peak in the age group of 30-39 years in case of males and 50-59 years in case of females. The cause of renal failure was slightly different in two sexes. Alports syndrome was responsible for ESRD in four of our male cases and three of them belong to same family. Collagen vascular disease was responsiole for ESRD in three of our female patients (2 had S.L.E. and one had scleroderma). Polycystic kidney disease was seen with equal frequency in both sexes but pyelonephritis (bilateral contracted kidneys seen on ultrasound) was seen in five of our patients. Diabetic nephropathy was the largest category seen in males. Diabetes is very common in this province (unpublished data under evaluation). About 20% of adult Saudi population is diabetic[1] and it is showing an escalating trend. With a very poor level of awareness and self care the magnitude of diabetic nephropathy is expected to increase in coming year. By for the maximum cases had no basic diagnosis in our patients. Common cause of ESRD in Asir region[4] has been glomerulonephritis followed by diabetes whereas in Gizan[5] it has been obstructive uropathy. Diabetes has also been reported to be the commonest cause of ESRD in Madinah al Munawarah[5]. Three of our patients had a failed kidney transplant.

Hepatitis C has been reported all around the world as main infection in ESRD patients causing considerable suffering in these already immunologically depressed patients. Prevalence rates ranging fromm 2.5% in Sweden to 28.8% in Portugal[6] has been reported from Europe. In

and around the Gulf countries also there has been many reports on this subject. Anti-HCV prevalence in haemodialysis patients has been 25.5% in Jordan[7], 40% in Kuwait[8], 44.6% in Qatar[9], 34.9% in Sudan[10], 40% in U.A.E[11], 80% in Egypt[12], and 35% in Morocco[13]. There are many single center, multicenter and national levels studies on prevalence of hepatitis C in dialysis patients in Saudi Arabia. Prevalence ranging from 15.4% - 94.7% is reported[14]. In our patients prevalence rates of 46.2% was seen which is less than 19 different centers in the Kingdom. Even those centers which has prevalence lower than our center had a very small number of total patients. We strictly follow universal infection control precautions in our unit. We are unable to isolate Anti-HCV positive patients due to multiple technical difficulties. Anti-HCV positivity was significantly higher in-patients above the age of 50 years and in those who had a longer duration on dialysis. Similar observation has been reported before also[15]. However there was no significant relation between the number of blood transfusion and anti HCV positivity. In fact our anti-HCV negative patient had received more transfusion than anti HCV positive patients. The possible reason could be that we had many new patients in this group who were given transfusions initially to stabilize them. Further all our blood is routinely screened for anti-HCV. We had only 7 patients positive for HbsAg (10.4%). The reason for this low rate as compared to anti-HCV could be that hepatitis B vaccination has been started in Saudi Arabia around ten years before as a part of universal immunization program and we vaccinate all our new patients as early as possible. We isolate all our HHbsAg positive patients. As mentioned we strictly adhere to universal precautions in dealing with our patients and that is recommended in all dialysis units specifically[16]. Disinfection methods have been studied and correlated with the propagation of hepatitis C in dialysis centers. We use following disinfection procedures in our unit. (a) For HD-Secura machines we perform decalcification using citric acid 50% for 21 minutes after every dialysis. Either chemical disinfection (by Puristeril 340 containing-peracetic acid 3.5 grams and Hydrogen peroxide 100 grams) or thermal disinfection is then performed daily. (b) For Fresenius 4008 machines chemcial disinfection by puristeril is used after every dialysis and thermal citric acid every week. (c) For Cobe-century-III acid rinse or Clorox disinfection is performed after every dialysis and formaline dininfection every week. Although it is reported that neither strict universal precaution alone nor chemical disinfection coupled with heat at 85°C for 35 minutes, was enough to stop the march of seroconversion.[17] Therefore we try to keep all our new machines for strictly Anti-HCV negative young patients.

Conclusion

ESRD is one of the chronic disease which needs continued care. Diabetic nephropathy is the commonest cause of ESRD in our male patients. In view of high prevalence of diabetes, this category is expected to show a steep increase in future for which we need to be mentally prepared. Hepatitis C continues to be the commonest infection in these patients and strict adherence to universal precautions combined with proper disinfection procedures are very important and might be sufficient to check its spread. Further research is needed to know the exact mode of transmission in this category of patients and methods to contain this infection.

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ROLE OF PROPHYLACTIC CRANIAL IRRADIATION IN SMALL CELL LUNG CANCER.

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ABSTRACT: *This study was conducted with an aim to analyze the impact of prophylactic cranial irradiation in small cell lung cancer with respect to brain relapse pattern and frequency, central nervous system toxicity and overall survival. A total of 40 patients enrolled for this study out of which only 21 patients, achieving complete remission, were taken up for the study. These 21 patients were divided into two groups of 11 patients (Study group) and 10 patients (Control group).*

Patients in study group were given prophylactic cranial irradiation using Co-60 beam to a dose of 2500 cGy in 10 fractions over 2 weeks. Patients were followed upto a maximum period of 12 months.

In study and control groups all patients (11 and 10) were alive upto six months of follow-up, 10 patients (90.90%) and 9 patients (90%) were alive at nine months of follow-up and 7 patients (63.63%) and 6 patients (60%) were alive at twelve months of follow-up.

One patient (9.09%) in study group and two patients (20%) in control group had central nervous system relapse. In study group two patients (18.18%) developed acute reactions in the form of nausea and vomiting and one patient (9.09%) developed memory loss and intellectual deterioration due to prophylactic cranial irradiation at 10 months of follow-up.

This study has not documented any significant impact on overall survival, but has definitely reduced the central nervous system relapse to a considerable level with an acceptable level of neuro-toxicity.

Key Words: *Small cell lung cancer; Prophylactic cranial irradiation; Brain metastases.*

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INTRODUCTION

Small cell lung cancer (SCLC) represents one of the 12 broad types of lung cancer as recommended by WHO (1977) and constitutes about 22% of lung cancer.[2] The biological behaviour of SCLC is quite different from other types of lung cancer with very short doubling time and rapid growth with a propensity for early and widespread metastates.[3] This variant of lung cancer is highly responsive and most sensitive of all to chemotherapy and radiotherapy with superior median and long term survival in patients with limited stage disease compared to extensive disease.[2] However, this improved survival has allowed new manifestations of the natural history of small cell lung cancer to become apparent, the most pronounced of which is an increased risk of the development of central nervous system metastases.[3] The frequency of central nervous system involvement is directly proportional to length of survival. But the data available presently does not predict individual relapse risk for these patients.[15] Central nervous system metastases are more common in small cell lung cancer (30%) than in other types of lung cancer,[3] and are an important cause of morbidity and mortality in patients with small cell lung cancer.[2]

Therefore, it becomes justifiable to decrease the central nervous system disease relapse especially in the light of increased CNS metastases with improved survival achieved with the advent and use of highly effective chemotherapeutic agents combined with thoracic radiotherapy in the overall management of small cell lung cancer.

The possible way out to reduce the central nervous system relapse is by using prophylactic cranial irradiation and its role is justified because small cell lung cancer is a systemic disease best treated by systemic chemotherapy,[1,7] but the sub-clinical disease in central nervous system is, however, in a sanctuary site protected by blood brain barrier. Thus, chemotherapy denies access in sufficient concentration to eliminate lurking small cell cancer.[7] Therefore, prophylactic cranial irradiation can eradicate this disease and so cure those patients who having achieved a complete response, would have relapsed in the central nervous system as the sole site of failure.[7]

Thus the rationale of prophylactic cranial irradiation is:

1. >60% complete remission rates achievable in limited stage small cell lung cancer but 30% patients relapse in brain.[3]

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2. Median survival improved in limited stage small cell lung cancer with systemic chemotherapy and thoracic radiotherapy, but with improved survival increased chances of brain metastases:
   (a) 60% have brain metastases in autopsy series.[14,19]
   (b) 80% have brain metastases if surviving for 2 years.[13,14,19]
3. Overt brain metastases cause morbidity, poor quality of life, poor symptom control and median survival of 2.5 months. We, therefore, undertook a randomized prospective study to evaluate the role of prophylactic cranial irradiation in limited stage small cell lung cancer.

MATERIAL AND METHODS

The study was conducted at Sher-i-Kashmir Institute of Medical Sciences, Srinagar (Kashmir), in the Department of Radiation Oncology and Medical Oncology. Out of a total number of 1809 patients attending the Department from March 1995 to April 1997, lung cancer constitutes approximately 9% and out of which approximately 34% was small cell lung cancer (SCLC). A total of 40 patients meeting the following eligibility criteria were taken-up for this study:

Eligibility Criteria:

1. Histopathological diagnosis of small cell lung cancer.
2. Age: should be less than 70 years.
3. Sex: both males and females were selected.
4. Performance status: stage zero and stage one (ECOG)
5. Limited stage disease: which was defined as disease confined to one hemithorax with or without ipsilateral or contralateral mediastinal or supraclavicular lymph-node metastases and with or without ipsilateral pleural effusion independent of cytology.[1,4,17]
6. No past history of any neurological disorder.

Patients fulfilling the above eligibility criteria were subjected to a pre-treatment evaluation which consisted of:

1. A complete medical history
2. A detailed physical examination
3. Haemogram
4. Liver function tests
5. Kidney function tests
6. X-ray chest (PA view)
7. Bronchoscopy
8. Bone marrow biopsy
9. Ultrasonography abdomen
10. CT Scan Brain to rule out presence of brain deposits.
11. CT scan chest was done as and when required.

Patients were subjected to a three phase treatment protocol which was as under:

Phase I:

All patients initially received three cycles of systemic combination chemotherapy every 21 days (3 weeks) in the form of:

a) Inj. Cisplatinum 30mg/m² day I, II, III.
b) Inj. Etoposide 100mg/m² day I, II, III.

Phase II:

On completing three cycles of combination chemotherapy, patients, were subjected to irradiation treating lung lesion and mediastinum on telecobalt 60 to a dose of 40 Gy in 3 weeks, 5 frs/week.

Phase III:

After completing radiation therapy to lung, a gap of two weeks was given, followed by three more cycles of systemic combination chemotherapy as in Phase-I.

Response Criteria:

The response to treatment was evaluated after completion of chemoradiotherapy (Phase I, II, III) and an assessment made as to whether a complete remission had been achieved. Complete remission was defined as complete clinical, pathological and radiological disappearance of all evidence of disease.[3,4]

Disease status was evaluated by physical examination, appropriate laboratory and radiologic investigation including a mandatory X-ray chest and C.T scan chest and head.

Patients who achieved a complete remission were divided into two groups: the Study group and the Control group on the basis of a blind draw.

The study group patients were subjected to phase IV of the treatment protocol which was prophylactic cranial irradiation.

Phase IV:

Prophylactic cranial irradiation using telecobalt-60 to a dose of 2500 cGy in 2 weeks, 5 frs/week.[18]

The patients in Control group were not given Phase-IV of treatment protocol and acted as a Control for comparison of the results.

RESULTS

A total of 40 patients with limited stage small cell lung cancer who fulfilled the eligibility criteria were enrolled for this study. Out of these only 21 patients, having completed the first three phases of treatment protocol, achieved complete remission. These 21 patients were divided into study group of 11 patients and control grou

of 10 patients (Table-I).

Table-I:

Total No. achieving complete remission	Study group	Control group
21	11	10

Patient characteristics were compared and evaluated between the two groups by means of statistical analysis (Table-II).

Table-II: Patient characteristics in Study and Control groups.

	Study group	Control group	p value
a) Mean Age	53.82±10.87	50.40±11.24	p>0.05(N.S)
b) Sex Distribution (M:F)	8:3	8:2	p<0.10(N.S)
c) Stage of disease	Limited stage	Limited stage	No difference
d) Performancestatus	Stage-I(ECOG)	Stage-I(ECOG)	No difference
e) LDH levels	Increased in one	Normal in all	Not significant

Patients in both groups were equally matched for age, sex, stage of disease, performance status and LDH levels.

The study group patients were given phase-IV of treatment protocol consisting of prophylactic cranial irradiation (Table-III).

Table-III: Prophylactic Cranial Irradiation (Phase-IV)

Equipment	*Theratron-780 (Telecobalt 60)*
Tumour dose	2500 cGy
No. of fractions	10
Dose per fraction	250 cGy
Duration of treatment	Two weeks (5 fractions/week)
Target volume	Whole brain
Portals used	Two lateral parallel opposing

Patients in both groups were closely followed at monthly intervals. In control group two patients had central nervous system relapse at 7 and 11 months of follow-up while one patient in study group relapsed in central nervous system at 12 months of follow-up (Table-IV).

Table-IV: Central Nervous system (Relapse pattern)

	Study group		Control group	
Time of follow-up	No.	%	No.	%
7 months	-	-	01	10
11 months	-	-	01	10
12 months	01	9.09	-	-

p value: Statistically not significant.

Though the results of central nervous system relapse pattern were not statistically significant but from a percentage point of view there was nearly a 50% reduction in the incidence of central nervous system relapse. Also, the control group patients relapsed earlier as compared to study group patients.

Central nervous system toxicity with prophylactic cranial irradiation was evaluated in study group. Two patients developed acute effects in the form of nausea and vomiting while one patient developed chronic (delayed) effects in the form of memory loss and intellectual deterioration.

Comparison of the survival between the study and control groups of patients showed that all patients in both groups were alive up to six months of follow-up, ten and nine patients at ninth month of follow-up and seven and six at twelth month of follow-up, respectively (Table-V and Figure 1). The survival difference between the study and control groups was not statistically significant.

Table-V: Overall Survival

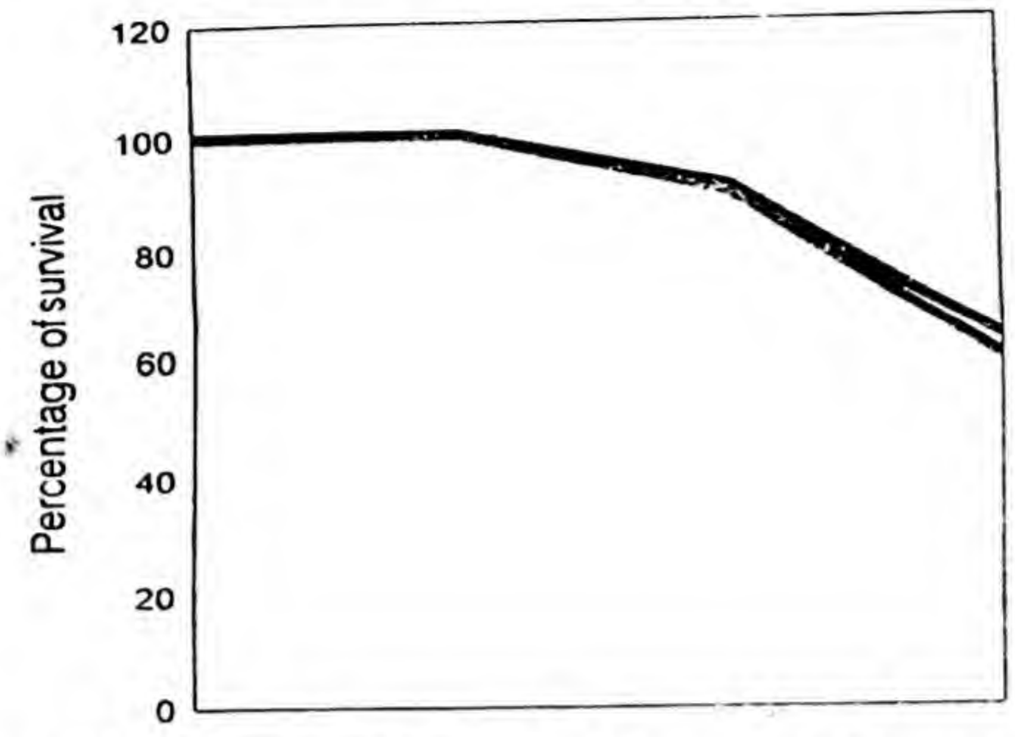
Folow-up (months)	Study group No.	%	Control group No.	%
At 03 months	11	100	10	100
At 06 months	11	100	10	100
At 09 months	10	90.90	09	90
At 12 months	07	63.63	06	60

DISCUSSION

Involvement of cranium in small cell lung cancer has been of known significance in the outcome of patient treatment for many years.[10] This is the variant which most commonly metastasizes to the brain and autopsy series have shown that multiple rather than single metastasis is the rule.[9] About 10% patients have brain metastases at presentation,[14] with increased frequency proportional to lengthening of survival,[9,7] approaching 50% to 80% in 2 year survivors without prior therapy to central nervous system.[14,19] Brain metastases are found in upto 65% of small cell lung cancer at autopsy.[14,19] Treatment of symptomatic brain metastases in SCLC with whole brain irradiation only occasionally yields significant palliation and this is usually a major cause of death in all.[9] Since approximately 30% of patients of small cell lung cancer relapse with brain metastases after achieving complete remission with systemic combination chemotherapy and radiotherapy to site of primary disease,[3] it becomes mandatory to decrease or to totally prevent such relapse from occurring.

Such reports led to pilot studies utilizing prophylactic irradiation of the brain.[10] However, the use of prophylactic cranial irradiation in limited stage small cell lung cancer

Fig 1: Overall Survial



remains controversial. Many of the earlier trials may be criticized for including mixed histologies, patients with extensive disease or patients never achieving a complete response in the thorax. Hence a definitive prospective trial incorporating limited stage cell lung cancer patients has not as yet been completed.[16]

In this study, patients after being subjected to a three-phase treatment protocol consisting of chemotherapy and external beam radiotherapy to primary lesion, were subjected to evaluation for having achieved complete remission. About 72.41% were found to have achieved complete remission, which was consistent with other reports.[6]

Achieving a complete response is essential because prophylactic cranial irradiation would only benefit patients in complete response.[5,10]

In our study, one patient (9.09%) from study group had central nervous system relapse at 12 months of follow-up while two patients (20%) in control group relapsed in central nervous system, one at 07 months and another at 11 months. The relapse rates in control group are consistent with rates reported in other studies.[11,12] whileas the nearly 50% reduction in relapse rate in study group was quite encouraging.

Acute toxicity due to central nervous system irradiation, which was reversible, did occur, but chronic (delayed) effects were seen in one patient (9.09%) only. However, any conclusions with regard to late effects (central nervous system morbidity) were difficult to arrive at party because of short survival and partly because of small number of patients.

We did see CNS toxicity in our study but considering PCI alone responsible for it would not be justified because a high proportion (97%) of small cell lung cancer patients with no focal neurologic findings have cognitive dysfunction even when not given brain irradiation and these deficits sugge t frontal subcortical dysfunction. This is also the region c ' brain involved in paraneoplastic limbic enceph alopathy.[13] Therefore, prophylactic cranial irradiation alone will not be a very strong factor responsible for any neurological manifestations, rather other etiological factors need to be kept in consideration as well which include neurotoxicity of multi-agent chemotherapy especially cisplatin and etoposide and paraneoplastic syndromes.[13]

The survival pattern in our study showed 100% survival in both groups upto six months of follow-up with a proportionate decrease after that till 12 months when the survival differences did not prove to be statistically significant.

Even if no improvement in survival is achieved but only a decrease in central nervous system relapse rates occurs, it is still beneficial for the patient in the long run because the patient is spared the neurologic complications of metastatic brain disease and the extra time, effort and expense of returning to the centre for therapeutic treatment of brain metastases.[10] Also the rapid deterioration of patients developing overt CNS involvement despite therapeutic CNS irradiation is strong argument for prophylactic treatment.[8]

CONCLUSION

In conclusion, in patients with limited small cell lung cancer achieving a complete response after systemic chemotherapy and thoracic radiotherapy, prophylactic cranial irradiation was associated with an acceptable degree of neurologic toxicity and an insignificant increase in survival as compared to patients not receiving prophylactic cranial irradiation. Therefore, role of prophylactic cranial irradiation in patients with limited stage small cell lung cancer (with complete response) needs further exploration in large prospective randomized studies because a decrease in relapse rates can translate into improved overall survival for these patients.

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CEREBROSPINAL FLUID CYTOLOGY IN "BRAIN TUMOURS" - A STUDY OVER A PERIOD OF 10 YEARS (1991-2000)

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ABSTRACT: *Tumour cells in cerebrospinal fluid were first reported in 1904 and metastatic carcinoma cells were recognised increasingly from 1908[1]. With advance in the neurodiagnostic techniques, most neurologists are reluctant to do a lumber puncture in patients with suspected brain tumours and are dependent on CT scan, MRI etc. etc. Cytological examination of CSF (cerebrospinal fluid) has its own role to play and has a great diagnostic utility in diagnosing, managing and monitoring the course of a leukaemia and lymphoma. It can also prove a good diagnostic tool in detection of carcinomatous meningitis and few primary brain tumours. Use of cell markers and cytocentrifugation technique by cytopathologists recently has improved its diagnostic utility and made it more acceptable diagnostic tool in brain neoplasia. Present study has been conducted with the aim of highlighting its diagnostic utility in suspected brain tumours and moreso in patients who cannot afford costly diagnostic procedures in a poor country like ours.*

Key words: *brain, tumours, cerebrospinal fluid,*

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MATERIAL AND METHODS

Present study was conducted over a period of 10 years (1991-2000) in the Department of Pathology, SKIMS, Soura, Srinagar. CSF samples from the admitted patients having high suspicion of brain tumour after careful collection, were immediately transferred to cytology laboratory for further processing. Smears were made from the deposit after samples were subjected to cytocentrifugation. Staining of smears was done by papanicolour stain and Geimsa stain.

OBSERVATIONS

In the present study, over a period of 10 years (1991-2000), 438 CSF samples from suspected brain tumour patients were examined microscopically for malignant cell cytology and following are some observations:-

Table 1:

Total No. of	No. of smears +ve for malignant cells	No. of smears -ve for malignant cells
438	114 (26%)	324 (74%)

Table 2:

Total No. of CSF samples	No. of CSF smears +ve for malignant cells	Primary brain tumours	Secondary brain tumours
438	114 (26%)	20 (17%)	94 (83%)

Out of 438 smears, malignant cells were present in 114 cases (26%) which included both primary as well as secondary brain tumours also.

Table 3:

Total No. of CSF smears +ve malignant cells	No. of cases with second--ary brain tumour	Nature of secondary brain tumours	No.
114	94	Acute lymphoblastic Leukaemia	38 (40%)
		Chronic myeloid Leukaemia	4 (5%)
		Lymphoma	24 (25%)
		Epithelial tumours	28 (30%)

Secondary brain tumours constituted 83% of the positive smears, out of which ALL constituted 40% of the cases followed by lymphoma 25% and epithelial cell tumour deposits in 30%.

Table 4:

No. of +ve smears	Primary brain tumour	Type of tumours	
114	20	Medulloblastoma	10 (50%)
		Astrocytoma	7 (33%)
		Ependymoma	3 (17%)

Out of primary brain tumours diagnostic yield for medulloblastoma was maximum (50%) of cases followed by high grade astrocytoma (33%) and lastly by ependymoma (17%) of cases.

DISCUSSION

Normal CSF should contain no more than 5 cells/mm of 10 cell/mm^3 in neonates. A normal centrifuged deposit shows a few lymphocytes, one or two polymorphs occasional histocyte and few ependymal or choroid plexus

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cells. CSF of both primary and secondary brain tumours usually contain leucocytes and malignant cells if they are in contract with CSF compartment.

In the present study, out of 438 CSF samples examined, 114 smears (26%) were positive for malignant cytology. In various studies conducted by Glass co-workers[2] and Bots et al[3] diagnostic yield of CSF samples in brain tumours was 6-% and 50%. Tumour cells are derived from both the leptomeningeal surface and form the parachymatous lesion. The ability to shed cells depends upon the cohesiveness of the cells e.g. squamous cells, carcinoma cells in CSF is rare[4]. Deep seated tumours probably enter the CSF compartment by direct extension or via the perivascular cuff or migration along the meninges.

In the present study, diagnostic yield in case of primary tumours is low (17%) compared to secondary brain tumours which continued in 83% of the positive smears. Other data available also reveal low cytodiagnostic yield in primary brain tumours than secondary brain tumours. Balhazin[5] and Gordon[6] had 15-30% diagnostic yield in primary brain tumours. Similarly Skye and Olischer[7] had a cytodiagnostic yield of 14% in primary brain tumours and 30% in secondary brain tumours.

Usually very few diagnostic cells are recovered in CSF samples. Presence of dense malignant cell population suggests a possibility of carcinomatous meningitis[8,9]. In the present study, out of 20 cases diagnosed to have primary brain tumours, 10 cases (50%) had medulloblastoma, followed by high grade astrocytoma (33%) and 17% cases had ependymoma.

Almost similar observations were recorded by Gondos[8] and King[10]. 61.9% in medulloblastoma, 28.6% in astrocytoma and 23% cases had ependymoma. Medulloblastoma, ependymoma and leukaemia shed the greatest amount of cellular material in CSF[11,12].

In the present study, 94 patients (83%) had metastatic brain tumours detected on CSF cytology. 38 cases (40%) had leukaemia, 24 cases (25%) had lymphoma and 28 cases (30%) had deposits from various epithelial cell tumours. Posner JB[8] also in a study observed presence of primary tumours mostly in breast lung and lymphoma with metastatic deposits in brain. On third of neoplasms having metastatic in brain could be detected by CSF cytology[2,10,12].

In the present study, diagnostic yield could have been better if multiple CSF samples were screened from a patient for tumour cytology. For better cytodiagnostic yield in case of brain tumours multiple CSF samples, good volume, even puncture higher up in cervical region is of great importance. Olson et al[12] in a study has concluded that multiple CSF samples from a patient when examined enhance their positivity. Other factors on which the positivity of a CSF sample depends include careful aspiration, proper preservation of sample, collection of a cells on cellulose membrane, cytocentrifugation[13], patency of CSF pathway, surgical intervention of brain tumours etc. etc. Faulty aspiration of nucleus pulposis can lead to false positive results. CSF is not a good medium for fragile tumour cells and contamination of samples can lead to false positive results[14,15]. Use of immunofluorescent stains, membrane antigens, cellular receptors are few new techniques in use which have increased the diagnostic yield of CSF samples and helped in tumour typing. 50% of patients with these methods were found to have increased number of leukaemia cells in absence of abnormalities[16,17].

It is concluded that CSF cytology is very good and cheap diagnostic tool for diagnosis of primary and secondary brain tumours.

Cytology of CSF determines the type of tumour on which depends the therapy and prognosis of patients which other techniques like CT or MRI cannot provide.

It has a key role to play in diagnosis, therapy and monitoring the course of a leukaemia and lymphoma.

Presence of malignant cells in CSF after surgery of a brain tumour indicates that abalative surgery is insufficient another therapeutic approach is necessary.

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A CLINICO-PATHOLOGICAL STUDY OF BREAST TUMOURS.

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Abstract: *A total number of 200 cases of breast tumours diagnosed histologically were studied. Of these 112 cases (56%) were carcinomas, 88 cases (44%) were benign. The tumours were classified according to WHO classification (11). Infiltrating duct carcinoma was found commonest histological type seen in 98 cases (89.5%)whereas, fibroadenoma was found commonest benign tumour found in 72 cases (36%). The rare lesion like squamous cell carcinoma was found in 2 cases (1.1%). Among the other individual tumours, lobular carcinoma 6 cases (5%); medullary carcinoma 2 cases (1.1%); Paget's disease 2 cases (1.1%) and cystosarcoma phyllodes malignant 2 cases (1.1%). The commonest side was left 80 cases (75.5%) and upper outer quardrant was found frequently involved 45%.*

The incidence of breast cancer was 4.4% of all the malignancies diagnosed histopathologically in the department during the same period.

KEY WORDS : *Breast tumours, Histopathology.*

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Introduction:

A lump in the breast is of great concern to the patient and also a challenge to the diagnostic acumen and judgement of the surgeon. Both the benign and malignant lesions present as lumps of variable sizes in the breast.Also the non-neoplastic lesions like traumatic fat necrosis,acute and chronic breast abscess, fibroadenomatosis and breast cysts usually present as space occupying lesions in the breast.It is therefore usually impossible to be sure about the nature of the lump.In many cases (estimated as 25%)even an experienced clinician cannot be certain about the diagnosis of lump inside the breast.Biopsy therefore assumes great importance(Bailey and Love,1975).

The present work has been undertaken to review and study the common morphological and histological types of breast tumours, their clinical presentation and relative incidence in this part of the country.

Material and Methods:

This study comprises of 200 cases of breast tumours received in the Department of Pathology, SKIMS over a period of 5 years from June 1995 to July 2000. These cases were analysed for various features, like age, clinical presentation, gross and histopathological appearances. Histologically these were classified according to W. H.O. Paraffin blocks were make from representative areas of the tumours. Sections were cut at 3-5 micron thickness and stained with haematoxylin and eosine. Where-ever required, special stains like periodic acid Schiff's stain and reticulin stains were also done.

Results:

200 breast tumours were studied during a five years period. Out of a total of 10000 surgical specimens. There were 200 breast biopsies constituting 2% of the total specimens. Amongst 10000 specimens, 2500 were malignant growths, out of which 112 different types of carcinomas of breast diagnosed histopathologically during the same period giving an incidence of 4.4% of all malignancies.

Histopathological spectrum of breast lesions:

Out of 200 cases of breast tumours, 112 cases were malignant and 88 cases were benign.

Hitological Type	No. of cases	%age
Carcinoma	112	56
Fibroadenoma	72	36
Fibrocystic disease	14	7
Papiloma	2	1%

The above table shows carcinoma ranks first in 112 cases giving an incidence of 56% of all the breast lesions studies. Whereas among benign tumour, fibroadenoma was commonest in 72 cases giving an incidence of 36%, cystic disease in 14 cases – 7%, papiloma in 2 cases giving an incidence of 1%.

Histological Typing of Breast Cancers:

Hitological Type	No. of Cases	%age
Infiltrating duct carcinoma	98	89.5
Lobular carcinoma	6	5
Medullary carcinoma	2	1.1

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Pagets disease	2	1.1
Squamous cell carcinoma	2	1.1
Cystocarcoma phyllodes	2	1.1

Age Incidence of Breast Tumours

Hitological Type	No. of Cases
Carcinoma	51.5 yrs
Fibroadenoma	25 yrs
Cystic Disease	40 yrs
Papiloma	30 yrs

Side of the Breast Affected

	No. of Cases	Percentage
Left Side	80	75.5%
Right Side	26	24.5%

Discussion:

The breast gland subjected to all physiological stress and strain undergo the pattern of histological changes which are faithfully mirrowed by corresponding clincial phenominon. This orderly physiological pattern continues uninterrupted from birth to death. This co-relation of clincial findings to histopathological features though outstanding in some conditions, is only poorly understood in others.

Age: The ensuing discussion is being conducted in respect of age and spectrum of different types of breast tumours. When age of the pateints afflicted with breast cancer is taken into account it was observed that disease is not seen in the prepubertal age group and there is no pateint among cancer patients studied below the age of 20 years. This is in confirmity with reports of Goldenberg [5] Baptist et al [1]; Haque et al [8].

Fibrocystic disease has been found at the age of 40 years in different series. In the present series mean age of the patients suffering from cystic disease is 40 years. This is in agreement with the observation of Jones [9]. Cystic disease is a disease of middle aged women. Platue of incidence at the age of 40 years suggest, that condition is due to hormonal imblance.

Fibroadenoma: The age at which fibroadenoma are commonly reported in literature is Haagensen [6] 33 year, between 21 to 25 years:- Haque et al [8] 23 years. In the present series fibroadenomas were found at the mean age of 25 years. The tumour chiefly occurs in the young woman, originating and growing during the years of sextual activity suggest, a changing pattern in the hormonal environment in this age group. The commonest symptom observed by different workers is the lump in the breast and less common is the retraction of nipple. In the present series commonest symptom observed was lump in the breast which approximates with the observation of Shapiro [12] reported relative risk of developing breast cancer is twice in unmarried than in married women and more in nonparous than parous. In the present series it has been observed that all malignant cases were married and all the patients achieved high parity having given birth to more than two children. Hence it is presumed that pregnancy and total parity does not seem to act as protective factor against development of breast cancer.

Side of the Breast affected:- Haagensen [7] reported that carcinoma of the left breast is more frequent than in the right breast. In the present series left side was involved more frequently than in the right.

Site within the Breast: Spratt et al (1967) described the relative frequency of carcinoma in different anatomic sites in the breast as:-

Upper outer quadrant	45%
Upper inner qudrant	15%
Lower outer quadrant	11%
Lower inner quadrant	5%
Central	25%

Almost half of the cancers begin in the upper outer quadrant of the breast. In the present study series 50% of the tumours were located in the upper outer quadrant which is in agreement with above mentioned workers and least affected was lower outer quadrant.

It may be argued that this quadrant contains a great bulk of breast tissue, than any other quadrant i.e., greatest number of centimeters of manmory gland exposed to risk of carcinomatous changes.

Histopathological Spectrum of Breast Tumours:

Bptist [1] reported after analysing 164 cases of breast lesions that carcinoma of the breat was the first lesion found in 61 cases (37%) of the total cases.

Haque [8] reported after analysing 200 cases of breast lesions that carcinoma of the breast was the commonest lesion found in 92 cases (46%) of these total breast lesions. In the present series of 200 cases of breast lesions that it has been observed that carcinoma of the breast ranks first found in 112 cases 56%. This is in confirmity with the observation of the above mentioned workers.

Histopathological Type of Breast Cancer: Baptist [1] reported infiltrating duct carcinoma was the commonest histological type seen in 81% of the total cases.

Haque A [8] reported infiltrating duct carcinoma was the commonest histological type seen in 75% of their cases. In the present series infiltrating duct carcinoma with preductive fibrosis was the commonest histological type found in 89% of the total breast cancer. This findings is in agreement with the above mentioned workers. Haque [8] reported that fibroadenoma as the commonest benign tumour in 55 cases (27%) of the total breast lesions. In the present study fibroadenoma has been observed to be the commonest benign tumour accounting for 72 cases (36%)of the cases. This is in confirmity with the above

mentioned workers.

The incidence of breast cancer was 4.4% of all the malignancies diagnosed histopathologically in the department during the same period. The incidence is in confirmity with Tyaqi [13] and Ready [10] who reported the incidence of 4.4 % to 16% of the breast cancer of all the malignancies.

Summary and Conclusion:

1. The present study consists of 200 cases of breast tumours. On the basis of analysis of these cases, infiltrating duct carcinoma was observed to be fairly common.
2. Amongst benign lesions, fibroadenoma was found to be commonest benign tumour next being fibrocystic disease.
3. Rare lesions like squamous cell carcinoma was found in 2 cases.
4. Commonest side effected was left accounting for 80% cases. Upper and outer corner of breast was involved frequently in 45% of cases. All the patiens presents with lump in the breast as chief complain. The patient with carcinoma presented with quite advanced stage as compared to observation of the western authors. This is because our patients being mostly illitrate, try to hide the lump untill it has acquired a large size.
5. The public education regarding significance of the lump in the breast and the need for early medical consultation is evident and this can be achieved through mass media and through various educational programmes.

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PREGNANCY WEIGHT GAIN IN RELATION TO VARIOUS SOCIOMEDICAL FACTORS AND PERINATAL OUTCOME

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Abstract: *The present study has been conducted in the department of obstetrics and community medicine. 260 primigravidae mothers from early pregnancy were registered and followed through their pregnancy till delivery. All mothers were free from any morbid condition. The relevant information on socio-medical parameters, nutritional status and biochemical investigations was collected every month. At term mode of delivery, neonatal outcome and nutritional status of newborn were recorded. The present study showed a mean weight gain of 7.9±2.1 kg (7.25-8.54kg 95% CI), which is better than some reported series. The better weight gain is attrbuted to better pre pregnancy weight (49.74±5.4kg) and comparable energy intake to RDA levels during pregnancy. The weight gain pattern showed initial rise up to 26 weeks with a further steep rise between 28-36 weeks and then a slowing down. The trimester wise weight gain showed .256kg/week in 2nd trimester and .34kg/week in 3rd trimester. only 28% mohers gained between 5-7 kg weight during entire pregnancy, rest all gained above that. Total weight gains correlated significantly with better SES, light physical work, age above 20 yrs, better caloric and protein intake in ithe deti (P<0.001). Multivariate analysis confrmed highest effect of maternal age, hemoglobin and caloric intake on total weight gain in pregnancy. The mean birth weight was 2.87±kg. Though various maternal variables affect birth weight, however multiple regresson analysis showed total weight gan as an important variable to influence birth weight. Total weight gain also influenced the mode of delivery in the present study. The study confirms dependence of Weight gain pattern on maternal socio-medical factors (age, caloric intake and hemoglobin levels) and effect of total weight igan on newborn birth weight and its out come. Thus attention to these factors in pregnancy ito improve the overall health of newborn and its out come has been stressed.*

Key words; *Pregnancy, Total weight gan, Birth weight, socio-medical factors.*

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Introduction

The course and outcome of pregnancy are influenced by the mother's nutritional status before conception, her diet during pregnancy, previous and concurrent disease and life style she adopts. Three major anthropometrics factors viz. maternal height, pre pregnant weight and gestational weight gain represent a combination of genetic and environmental influences. Although each factor independently influences birth weight and length of gestation, the effects are neither equal nor additive[1]. Perhaps the most astonishing finding about weight gain in pregnancy is the range with whch that is compatible with clinical normality in pregnancy and a normal outcome. On the whole there appears to be no unanimity regarding the deal weight gain in pregnancy, the usual weight increase is stated to be 25% of initial body weight. Thus the expectant Indian women should put on 10kg during gestation[2]. The mean gain in body weight from the 12th to 40th week of gestation was however found to be only 6.02±0.377Kg[3].

A linear relation ship exists between a mothers weight gain during her pregnancy and her newborn baby weight. It is reasonable to assume that prenatal nutrition may be prime determinant of maternal weight gain and consequent newborn full term weight[4]. Maternal weght igan during pregnancy is a major indicator of birth weight, a primary indicator of infant mortality and morbidity[5]. The variations in the weight gain during pregnancy and lack of ideal data in this part of country initiated this preliminary study to know the weight gain pattern during pregnancy and their impacts on pregnancy out come.

Methodology

The present study was a longitudinal, prospective study of healthy normal primigravida followed from first trimester up to delivery which was conducted in the department of obstetrics and community medicine SKIMS, Srinagar from May 1997 to 1998. All primigravidae mothers attending antenatal clinic were included in the study. Only primigravidae with singleton pregnancy and normal course were taken up for the final study. The study excluded all mothers who developed any pathology during course of gestation likely to influence the weight gain or fetal growth.

Of the randomly enrolled initial sample of 260 mothers, only 150 mothers had regular monthly follow up with total

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compliance to various investigations. All the relevant socio-medical characteristics of mothers including physical activity, dietary history has been collected as per the schedule designed for the purpose. The mothers were subjected to general physical examination, obstetric examination, anthropometric assessment and requisite lab investigations as per standard methods. The mothers were followed for their final outcome and the newborn were subjected to anthropometrics for growth assessment.

The data thus collected has been analyzed on SPSS software package mainly for correlation (r), regression and analysis of variance, R^2 values of regression coefficients, standard errors of these estimates and their corresponding P values.

Results:-

Table-1: Weight gain patterns at different gestational ages

Gestational Age	Wt. gain Kg/month	Wt. gain Kg/week	% Increment	Cumulative frequency of % Wt. Gain.
<16 WKS	0.30	.02	3.79	3.79
16-20 WKS	1.02	0.25	12.80	16.59
20-24 WKS	1.06	.26	13.40	29.99
24-28 WKS	1.12	.28	14.15	44.14
28.32 WKS	1.60	0.40	20.24	64.38
32-36 WKS	1.50	.37	18.96	83.34
36-40 WKS	1.31	.32	16.66	100.0

Total weight gain pattern in the present study shows a negligible increase of .3 kg/month up to 16 weeks (3.7% of total weight gain) thereafter almost 1 Kg/month can be seen upto 24.28 weeks (12.8 to 14.15% increase of total weight gain). At 28 weeks Gestation there is a sudden increase of 1.6 Kg/month (20.24% increase of total weight gain), which continues to 1.5 kg/month at 36 weeks (18.96% increase), thereafter there is a slight decline in weight gain reaching to 1.4 Kg/month at 40 weeks of gestation.

Table-II: Weight gain in different trimesters.

Timester	Mean wt gain Per/Wk	Per/Mon	S.E Increment	95% C.I	%
1st	.02	.30±48	.0379	.1997 to .3479	3.79
2nd	26	3.15±1.07	.0877	2.98 to 3.32	39.8
3rd	.37	4.47±1.04	.0856	4.30 to 4.46	56.58
Total	*7.9±2.1*		*.106*	*5.83 to 9.97*	*100*
Weight Gain					

Trimester wise again only .3Kg increase (which is 3.7% of total weight gain) is seen in first trimester, followed by 3.15 kg±1.07 (which is 39.8% of total weight gain) in second trimester and 4.47 Kg ± 1.04 (which constitutes to 56.58% of total increase) in last trimester.

Most of the maternal variables affected the weight gain in mothers during pregnancy, however significant positive correlation of maternal height (r=.5707), maternal Hb (r=.4764), caloric intake (r=.4565), WHPI (r=.4404), MAC (r=.4354), age (r=.4166), and pre pregnancy weight gain (r=.3702) in that order was seen. There was no correlation between WHRI, and serum albumin levels with the weight gan patterns.

Table-III: Multiple Regression Analysis

Dependen variable — Total Weight Gain
Multiple R of the equation
P- value of Regression model setting:- P<0.0001

Variables	Regression Coefficient	Stand Error	T-Value	P-Value
Age	.174813	.3879	4.5	.0000
Height	.3317	.2693	1.23	.22
MAC	.1485	.1083	1.37	.172
WHRI	-1.035	198.46	-.408	.68
WHPI	-.557	.608	-.917	.36
Pre-Pregnan Weight	1.58	2.15	.732	.465
SA mg%	.1246	.553	1.40	.182
Hb mg%	.407	.123	3.287	.0013
Caloric Intake	2.237	.550	4.056	.0001
Protein	1.92	.2535	.835	.501

The multiple regression analysis between total weight gain presented in the table shows r2 of the equation as 0.5417 (P<.0001). After controlling other variables (regression analysis) only maternal age (P<.0001), hemoglobin (P<.0001) and dietary caloric intake (P=.0001) were found to significantly affect total weight gain. The r2 of the model predicts that 54% of the variation in gestational weight gain is because of these factors.

Table-IV: Gestational weight gain, mode of delivery and type of weight gain

Total Weight Gain	Mode of delivery Normal	LSCS	Type of delivery Pre term	Term	Post term
<5	13(13.45)	0	4(30.76)	9(69.23)	0
5-7	32(33.33)	7(12.96)	4(10.25)	28(71.79)	7(13.94)
7-9	37(38.54)	22(40.74)	1(1.69)	45(76.75)	13(22.03)
>9	14(14.58)	25(46.29)	0	23(58.97)	16(41.02)
Overall	96(64%)	54(36%)	9(6)	105(70)	36(24)
			t=6.76, p<.0001		t=5.27, p<.001

The table shows that 64% mothers had normal vaginal delivery and rest and delivered abdominally (LSCS). Mothers who gained >9 Kg weight during entire pregnancy had highest 46.29 percentage of LSCS mothers gaining between 7-9 Kg with 40.74% and the lowest the lowest percentage 12.96% being among mothers gaining during 5-8 kg weight during entire pregnancy.

Overall 70% of the registered mothers delivered at term and 24% delivered post mature while 6% delivered pre term. The percentage of pre term deliveries was high

(30.76%) with <5kg weight gain during pregnancy and the percentage of post term deliveries was more (41.02) with >9 Kg weight gain.

Table-V: Weight gain in relation to Birth weight and prevalence of low birth weight.

TWG		Birth Wt Distribution				LBW	Prevalence of LBW
	n	<2	2-2.5	2.5-3	>3	(n)	
<5	13	5(38.46)	7(53.84)	1(7.690)	0	12	92.66
5-7	39	2(5.12)	18(46.15)	18(46.15)	1(2.56)	20	51.28
7-9	59	0	6(10.16)	41(69.49)	12(20.33)	6	10.16
>9	39	0	0 7(17.94)	32(82.05)	0	0	
Overall		112	(74.67)			38	25.33

The overall incidence of Low Birth weight in the present study was 25.3%. Mothers with low weight gain (upto 5 kg) had LBW incidence of 91.66% which dropped down to 51.28% among mothers gaining weight between 5-7 kg and 10.16% among mothers who gained between 7-9 kg. The birth weight in relation to maternal weight gain showed that mothers with low weight gain (up to 5 kg) had higher prevalence of babies between 2-2.5 kg (54%) and mothers gaining >9 kg weight during pregnancy did not gave birth to babies with <2.5 kg birth weight and conversely large percentage (82%) babies had >3 kg birth weight.

Table-VI: Relationship between maternal weight gain and neonatal anthropometry

Total weight gain	n	Birth Wt.	CHL	MAC
<5	13	2.16=0.46	41.5+1.07	7.8+0.69
5-7	39	2.51+0.24	43.10+1.7	8.47+0.45
7-9	59	2.80+0.26	44.99+1.89	9.12+0.42
>9	39	3.52+0.42	47.47+2.52	9.98+0.66
Overall		2.87	44.84	9.06
Regression Coefficient		1.920	-.001	.920
S.E		.353	.064	.253
t-value		5.43	.023	3.631
p value		.000	.9817	.0031

R^2 of equation =.7132
P <.001

The table shows that as the gestation weight advances, the neonatal anthropometrics also increases with best nutritional status been seen in infants of mothers who gain >9 Kg weight during pregnancy showing neonatal Weight of 3.52 Kg, CHL 47.47 cms and MAC 9.98 cms. Using multiple regression analysis, it is seen that maternal weight gain has statistically significant effect on Birth weight (p<.000) amd Mac (p<.0031) but not on CHL (p<.98).

The table shows that once the other factors are adjusted, the highest correlation was seen between the total weight gain and the birth weight (p<.000), and caloric intake and the birth weight (p<.000). Other factors were not found to have significant effect on the birth weight in the present study. The R^2 of the model which is 0.7132 explains that these factors are able to explain 715 of the variation in the birth weight.

Table-VII: Multiple regression analysis of birth weight in relation to maternal variables

Maternal Variables	Regression Coefficient	Standard Error	t-value	P-value
Age	.0066	.008	.788	.4322
Height	.0278	.054	.509	.611
MAC	.0334	.022	1.518	.131
WHRI	43.04	40.13	1.073	.285
WHPI	0.110	.123	.893	.373
PPW	.422	.437	.966	.335
SA	.422	.437	.966	.335
Hb	.034	.025	.940	.349
TWG	.185	.017	10.868	.000
Caloric intake	.175	.016	9.80	.000
Protein intake	.005	.007	.750	.3322

R^2 of equation = .726
S.E. = .295
P value of equation <.0000
Dependent Variable = Birth weight

Discussion

The mean total weight gain during entire pregnancy in the present study was 7.9±2.1kg , which is approximately 16% of the pre pregnancy weight. This is lower to the western weight gain of 14.9 to 16.1 kg repored by Johnston et al[6] and 16.7±5.0kg by Abrams and Selvin[7], yet it corresponds to Tripathi's weight gain of 8.3±1.1 kg and is better to 5.34±0.75 kg weight gain reported in South India studies[8]. Percentage weight gain observed by Shah & Shah was 10-15% over pre pregnant weight[9]. Gestation wise weight gain showed a near 'J' shaped pattern with a slow increase up to 26-28 weeks followed by a steep rise between 28-36 weeks. Even this pattern of weight gain is definitely better than the monthly weight gain observed by Venakatachalan[3] among primigravid mothers.

The trimester wise break down of weight gain shows a significantly varying pattern from 0.3±0.48 kg (.02kg/week) in first trimester to 3.156±1.07 kg (.26kg/week) in second trimester and 4.47±1.04 kg (.34 kg/week) in third trimester which constitutes only 3.79% increase in 1st trimester compared to 39.8% and 56.58% increase in 2nd trimester and 3rd trimester. These figures are not consistent with western literature, which showed an almost uniform gain in 2nd and 3rd trimester[10]. This can be attributed to no seriousness towards early pregnancy and physiological changes leading to reduce intake of food. Shah and Shah[9] reported a weekly weight gain of .14kg/week from 12.16 weeks and .17kg/week from 17 weeks onwards. In the present study 2/3rd mothers (65.33%) had gained 7-9kg of weight during pregnancy and 1/4th (26%) gained between 5-7kg as against the 39.5% and 39.75% respectively observed by Tripathi[8].

The significant difference in the strength of correlation with weight gain once arranged in raking order highlighted that the maternal height, hemoglobin, caloric intake and WHPI as the main four parameters in that order followed by MAC, age and prepegnancy weight of mother whcih influence total weight gain during pregnancy. The coefficient of correlation (r value) between various variables and weight gain varied between .51 to .37 in the present study which has eqully been shown to vary by other authors also. Once other variables were controlled (by regression analysis) only maternal age, hemoglobin and dietary caloric intake were found to have a significant effect (P<.0001) on weight gain. The R^2 value of .5417 in the model explains 54% variation in gestational weight gain attributable to these factors.

Various maternal variables studied in the present study showed a significant positive correlation with anthropometrics parameters of the new born of which birth weight showed significant (P<.0001) highest correlation with total weight gain. By applying multiple regression analysis between maternal variables and birth weight, the R^2 of the equation was .726 i.e. 72% of variation in birth weight could be explained by maternal variables. It was also evident that the total weight gain during pregnancy has the highest bearing on birth weight in this population. Abrams and Laros[11] also reported that the maternal weight gain had a gereater impact on babies born to under weight women whereas Shah and Shah (Loc it) did not found any significant correlation between maternal weight gain and birth weight.

The overall incidence of LBW in our study was 25.3% that has shown a declining trend with increase in the total weight gain thereby showing that as the total weight gain improves the incidence of LBW reduces. lawoyin[12] also reported that all mothers who gained <5 kg gave birth to LBW babies. Tripathi[8] observed 61.5% prevalence of low birth weight babies among mothers with total weight gain of 5 kg or less compared to 36% in mothers gaining total weight gain of 7-9 kg.

A linear trend was observed between gestational weight gain and birth weight. Using multiple regression analysis, it was found that a unit change in maternal weight caused an icnrease in birth weight by 214+19 kg (P<.001) (diagram)

The pregnancy outcome showed that mothers with >9kg weight gain during pregnancy were significantly more likely to deliver by LSCS as compared to those who gained <5kg. The risk of delivery by LSCS among mothers gaining between 5-7 kg was only 1.55 times compared to 2.78 among mothers gaining >7kg or 3.39 among gaining >9 kg weight. Similarly, pre term deliveries were more common among mothers with weight gain <7kg. Parker and Abrams[10] reported a 20-30% increase in caesarean deliveries with high prenatal weight gain.

Thus the study reveals that in the present population total weight gain is governed by socio-medical factors like age of mother at conception, caloric intake and hemoglobin levels during pregnancy and in turn it determines the pregnancy outcome and birth weight. It would be important to lay stress on the measures, which would prevent conception at young age, improve caloric intake in pregnancy and raise hemoglobin levels in pregnancy.

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INTRAUTERINE MIDGUT VOLVULUS WITHOUT MALROTATION

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Abstract: *We are reporting a case of intrauterine midgut volvulus in a preterm baby who presented with fetal distress needing delivery by cesarean section. The baby was found to have abdominal distension, blue discoloration and induration of the abdominal wall and features of intestinal obstruction. Emergency laprotomy revealed midgut volvulus without malrotation. A large portion of the midgut was resected and ileostomy performed. She was also treated for the moderate degree of hyaline membrane disease. Total parenteral nutrition was given till oral feeding was established. Ileostomy was closed at the age of 48 days. The baby is growing well on oral feeds. To our knowledge this is the first case report of intrauterine midgut volvulus from the Kingdom of Saudi Arabia.*

Key Words: *CTG- Cardiotocogram.*

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Introduction:

Midgut volvulus most commonly occurs in the first year especially in the first months of life[1]. Midgut volvulus presenting before the age of one year has a higher incidence of morbidity and mortality[2,3]. Midgut volvulus occurring antenatally is a rare occurrence[4,5]. The outcome depends on the gestational age at the time of occurrence and the length of gut involved[6]. Although no specific clinical presentation is known fetal distress particularly decreased fetal movements, polyhydramnios and dilated intestinal loops are commonly present. Only 18 cases of intrauterine volvulus have been reported in the world literature with 12 survivals [4-17].

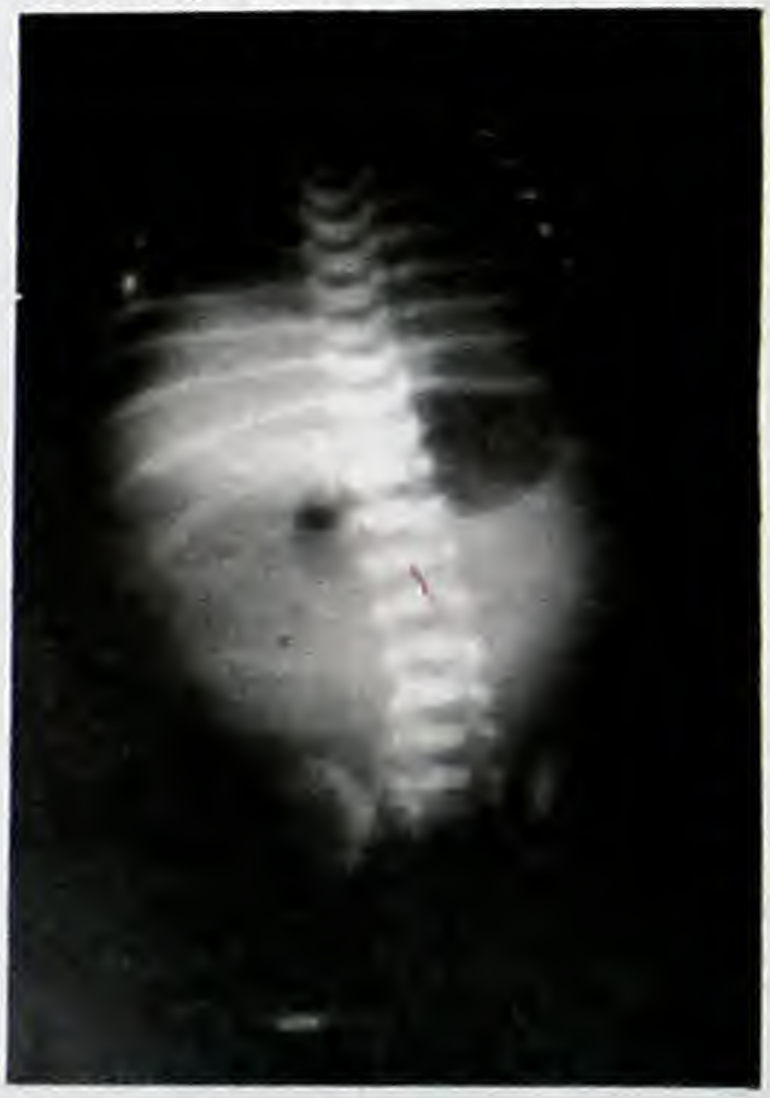

Figure-1: Plain X-Ray of abdomen Showing gas shadow up to the second part of the duodenum only suggesting obstruction at that level.

Figure-2: Peroperative Photograph showing the twisted and gangrenous mid gut.

Case summary:

A 29 years old Saudi lady presented with a 36 weeks gestation and history of decreased fetal movements. Cardiotocography (CTG) showed decreased fetal heart rate variability. A female baby was delivered by emergency cesarean section. Her apgar score was 1 and 6 at 1 and 5 minutes. She was resuscitated and ventilated at birth and admitted to Neonatal Intensive Care Unit (NICU).

The mother is gravida-8 and para-6 with 2 abortions. All her previous deliveries were normal and all the children are alive and healthy. She had regular antenatal checkups. Ultrasound done at 25 weeks of gestation was reported

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normal. Four days before delivery she noticed decreased fetal movements. She reported to the hospital where she was reassured after a routine checkup.

The baby weighed 2200 grams and gestational age was 36 weeks by assessment. Pulse rate was 140/minute and blood pressure was 74/36 mm. Hg. She was ventilated since birth, with high inspiratory pressure.

Initial Blood gas showed pH 7.27, Pco2 of 46 mmHg. and serum bicarbonate of 18 m mol. / liter.

Abdomen was markedly distended. Abdominal wall was discolored blue, indurated and tense on palpation. No abdominal organ or mass could be palpated. She had normal female genitalia and anal opening with free passage of meconium.

X-Ray of abdomen showed generalized radio-opacity with intestinal gas visible up to the second part of duodenum only. No free gas or calcification was seen in the abdomen. (Fig. 1) Chest X-Ray showed features of moderate hyaline membrane disease.

Ultrasound scan of the abdomen showed normal liver, spleen and both kidneys. No encysted fluid was seen. Heteroechogenic free fluid was seen in the abdomen. Peritoneal aspiration revealed blood-stained fluid. The peritoneal aspirate was sterile on culture.

Brain ultrasound and echocardiography were normal.

The patient was taken to the operating room with the diagnosis of intestinal obstruction probably due to volvulus. Laprotomy showed midgut volvulus and gangrene of gut involving ileum and caecum with ileal perforation. The caecum was mobile but there was no malrotation (Fig.2). The gangrenous ileum and caecum were resected and ileostomy performed. About 60 cm. of small gut was preserved. The colon was brought out as a mucous fistula. Histopathological examination of the excised bowel was

TABLE:- I LIST OF CASES OF ANTENATAL VOLVULUS DESCRIBED IN THE LITERATURE TILL DATE:

Case No.	Author and year of publication	Gestational age in weeks	Fetal monitoring findings	Antenatal Ultrasonography	Mode of Delivery
1.	Seward J Zusman J. 1978 [7]	—	———	Hydrops Fetalis	——
2.	Baxi et al 1983 [8]	34	Normal	Polyhydramnios Ascites, Abdominal mass	Spontaneous
3.	Samuel et al 1984[9]	34	Normal	Abdominal mass Polyhydramnios	Cesarean section
4.	Nogami et. al. 1985[10]	—	———	Hydrops Fetalis	——-
5.	Witter & Molteni 1986[11]	34	Fetal movements Variability on CTG	———	Cesarean section
6-9.	Ashworth T. 1988[12]	19-22	Necropsy findings	———	Spontaneous Abortions
10.	Ho et al 1990[13]	35	Fetal movements	Dilated intestines Ascites	Cesarean section
11.	Suzumori et al 1990[14]	36	Variability on CTG	Polyhydramnios Abdominal mass	Cesarean section
12.	Usmani and Kenisberg, 1991[15]	29-30	———	Polyhydramnios	Spontaneous
13.	Usmani and Kenisberg,1991[15]	34	Fetal movements	———	Cesarean section
14.	Black et al 1994[4]	34	———	Dilated Intestines	Spontaneous
15.	Felice et al 1997[16]	29	Normal	Dilated Intestines	Spontaneous
16.	Craig S. Easton M. 1998[17]	35	Fetal Movements Variability on CTG	———	———
17.	Crisera AC et al 1999[6]	37	Normal	———	Spontaneous
18.	Morikawa N et al 1999[5]	31	Fetal movements	Dilated Intestines	Cesarean section
19.	Current Case 2000	36	Fetal Movements Variability on CTG	———	Cesarean section

TABLE- II: NEONATAL FINDINGS IN THE SURVIVING CASES OF INTRAUTERINE VOLVULUS

S. No.	Sex	Gestational Age in weeks	Birth weight in Grams	Mode of Delivery	Symptoms and signs	Associated Lesions
1.(8)	F	34	2200	Spontaneous	Abdominal Distension	Nil
2.(9)	—	34	——	Cesarean section	Abdominal Distension Abdominal Mass	Peritonitis
3.(11)	F	34	2200	Cesarean section	Abdominal distension Cullen's sign, Anemia	Respiratory distress Hemoperitoneum
4.(13)	M	35	2398	Cesarean section	Abdominal distension Cullen's sign, Anemia	Respiratory distress Hemoperitoneum
5.(14)	M	36	2820	Cesarean section	Abdominal distension	Respiratory distress
6.(15)	F	29-30	1200	Spontaneous	Abdominal distension	————
7.(15)	F	34	1800	Cesarean section	Abdominal distension Cullen's sign, Anemia	Respiratory distress
8.(4)	M	34	2170	Spontaneous	————	———
9.(16)	F	29	970	Spontaneous	Abdominal distension	———
10.(17)	—	35	——	————	Abdominal distension	————
11.(6)	F	37	——	Spontaneous	Abdominal distension Cullen's sign, Bloody stool	Respiratory distress Malrotation
12.(5)	F	31	1774	Cesarean section	Abdominal distension Bloody stool, Anemia	Respiratory distress Hyperbilirubinemia
13.	F (Current Case)	36	2200	Cesarean section	Abdominal distension Cullen's sign	Respiratory distress

normal other than the findings suggestive of gangrene.

The patient had a smooth post-operative course. She was extubated at the 6th day of age. Total parenteral nutrition was started on 3rd post-operative day. Feeding was started on 7th post-operative day, increased gradually to full feed orally when parenteral nutrition was discontinued. Patient was discharged from the neonatal unit on the 21st day on predigested milk formula.

Discussion:

Eighteen cases of intestinal volvulus occurring antenatally have been reported so far (Table-I). Four of these were incidental autopsy findings in 19 to 22 weeks' gestational age abortuses[12]. Two other cases were associated with hydrops fetalis and died [7,10]. Of the 12 cases that survived 6 had features of fetal distress in the form of decreased fetal movements and / or abnormal CTG's. Four cases had normal CTG while in 2 others the information about fetal monitoring was not available. Six of the cases needed delivery by cesarean section, 5 of them for fetal distress and one for the diagnosis of intestinal obstruction and volvulus at 34 weeks of gestation by antenatal ultrasound[9]. The other cases delivered spontaneously at 29 to 37 weeks of gestation. Antenatal ultrasonography showed polyhydramnios in 4, dilated intestinal loops in 4, abdominal mass in 3 and ascites in 2 cases. (Table- I)

Among the 12 cases that survived 7 were females and 3 males. In two others the sex is not mentioned. The gestational age ranged from 29 to 37 weeks with a mean gestational age of 33.73 weeks. Eight of the 12 survivors (66%) were 34 to 36 weeks by gestation. Only one case of intrauterine volvulus was reported in a term baby[6]. Birth weight ranged from 970 grams to 2820 grams the mean weight being 1948 grams. The clinical findings observed were abdominal distension, Cullen's sign, anemia, bloody stool and hemoperitonium.

Our patient had many features similar to these described cases. The patient developed fetal distress in the form of decreased fetal movements and abnormal CTG. Post-natally she showed signs of intestinal obstruction with features of gangrene of the gut.

The gestational age at the time of occurrence of volvulus and the length of intestine involved in the event are the two important variables that determine the outcome[6]. Some investigators have postulated that volvulus occurring in the early fetal life and involving a short segment of intestine

that is nipped off could be a cause of intestinal atresia presenting in the neonatal period[12,15]. It is also postulated that midgut volvulus involving a major portion of intestine occurring in early gestation can lead to fetal loss. On the other hand a major volvulus occurring later in gestation may induce premature labour. Felice et. al. found a significant relationship between antenatal volvulus and prematurity as compared to postnatal volvulus.

They have postulated that fetal distress caused by volvulus induces release of both placental and fetal adrenal and hypothalamic stress hormones leading to premature uterine activity and preterm delivery[16].

The other important factor to determine the outcome in antenatal volvulus is the fetal maturity at the time of the event as it has a bearing on the severity of the problems related to preterm delivery and prematurity. In our case the patient was fortunate to be near term at the time when she developed volvulus.

From these reported cases we can formulate a set of prenatal signs of in-utero volvulus. In most of the cases with available data fetal distress particularly decreased fetal movements and poor heart rate variability were noted. Polyhydramnios, abdominal distension, abdominal mass, dilated intestinal 'oops and fetal ascites were other findings on antenatal ultrasonography (Table- I). In the cases that survived abdominal distension, Cullen's sign, and anemia were common (Table- II). Among the associated findings respiratory distress, hemoperitoneum, peritonitis and hyperbilirubinemia were noted. The association of polyhydramnios could be explained by the complete intestinal obstruction caused by the volvulus. Samuel et al have suggested that antenatal ultrasound would be a useful diagnostic tool. They found a static abdominal mass with dilated intestinal loops in their reported case[9].

However in spite of these signs occurring in many patients still there is not a sensitive and specific set of clinical signs that would make the diagnosis of antenatal volvulus possible with certainty. The aim of our presentation is to increase the awareness of intrauterine volvulus among obstetricians perinatologists and the neonatologists. The index of suspicion in the right setting should be high and a laparotomy should be done before detailed diagnostic tests. A normal plane X-Ray of the abdomen and enema may lead to delay in diagnosis resulting in an extensive ischemic necrosis of the bowel[15]. These preterm babies also need respiratory support in the form of artificial ventilation and surfactant therapy. In some cases abdominal paracentesis may be helpful temporarily by decreasing intra-abdominal pressure and enhancing ventilation[16].

Nobuyuki et. al . described a case of antenatal volvulus that showed a semicircular defect of intestinal muscle which could be secondary to the volvulus[5]. Similarly defects in mesentery have been reported with intrauterine volvulus[4]. In our case no underlying predisposing cause was identified.

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RETROSTERNAL GOITER –PRESENTING AS SUPERIOR-VENACAVAL OBSTRUCTION

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ABSTRACT: *A case of superior venacaval syndrome because of cervical toxic multinodular goiter with retrosternal extension occurring in a female described because of rare occurrence*

KEY WORDS: *Superior vena caval syndrome, Toxic multinodular goiter, Retrosternal goiter*

JK-Practitioner 2002; 9(2): 114-115

INTRODUCTION:

Superior vena caval syndrome (SVC) is usually an obstructive oncological emergency. Majority of cases are because of Malignancy (90%) and Benign causes are only 10%. One of the benign and rare cause is Retrosternal Goiter[1]. We are reporting a case of superior venacaval syndrome because of toxic nodular cervical goiter with retrosternal extension.

CASE:

A 60 year old female, ex-smoker from a remote area of Kashmir valley and with history of chronic asthmatic bronchitis presented to SMHS hospital in the department of Medicine with the chief complaints of palpitations, exertional as well as at rest of three years duration, heat intolerance, nervousness, increased sweating, tremulousness of both hands, fatigue, headache, giddiness, neck and facial swelling especially around eyes, breathlessness, cough, hoarseness of voice, nasal congestion, tongue swelling, dizziness and lethargy and syncope especially aggravated by bending forwards. There was no history of dysphagia, fever, epistaxis, and pain in the neck. Physical exam of the patient revealed congested cyanotic hue suffused and edematous face, edema of arms and chest, proptosis, glossal and laryngeal edema and mental obtundation, dilated neck veins, increased number of collateral veins covering anterior chest wall, thyromagaly, which is soft to firm moving with deglutition and lower edge of the gland is not felt with palpation, fine tremor in both hands with a resting pulse rate of 120 / minute without other signs of thyrotoxicosis. Pembertons sign was present i.e.; Veins become more prominent on raising hands above the head. There were distended non –pulsitile veins on neck and upper chest anteriorly and both upper arms with flow above down. The veins did not collapse on lifting arms up. Positive investigation of this patient revealed chest X-ray showing superior mediastinal widening and tracheal compression. FNAC (Fine needle aspiration cytology) revealed adenomatous colloid goiter, thyroid function tests (TFT) of this patient showed T3 and T4 raised. Iodine ^{131} uptake studies were not done. PFT (Pulmonary Function Tests) showed obstructive pattern. Keeping this data in view the diagnosis of Toxic multinodular goiter with retrosternal extension causing superior vena caval syndrome was made.

DISCUSSION:

Normal thyroid gland, a homogenous structure weighs about 20 grams. Goiterse is defined as thyroid enlargement at least two times the normal[2]. Superior venacaval syndrome is the clinical expression of obstruction of blood flow through SVC. First case of SVC syndrome was found in 1757 that had syphilitic aortic aneurysm[3]. In 1954 Schechter reviewed 274 cases of SVC and 40% of which were due to syphilitic aneurysm or tuberculous mediastinitis.[4] SVC is a major drainage vessel from head ,neck, upper extremities and upper thorax. It is located in middle mediastinum with a length of 6-8 cms and its breadth is about 1.5 X 2 cms. It extends from junction of right and left innominate vein to right atrium with distal two cms in pericardial sac. Azygous vein enters SVC posteriorly above pericardial reflection. SuperiorVenacaval Syndrome is an obstructive oncological emergency and is clinical expression of SVC obstruction with reduction in venous return from head, neck and upper extremities [5]. 90% of SVC'S are malignant, lung cancer, small cell constitutes 85%. Rest by lymphoma and metastatic tumors from testicular and breast carcinoma. Benign causes constitute about 10% including benign tumors in mediastinum, aortic aneurysm, thyroid enlargement, thrombosis of SVC, fibrosing mediastinitis due to irradiation or histoplasmosis or tuberculosis mediastinitis[6,7]. Clinically patients present with neck and

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face swelling especially around eyes. Dysponea, cough, and other symptoms like hoarseness of voice, tongue swelling, headache, nasal congestion, epistaxis, hemoptsis, dysphagia, pain, dizziness, syncope, and lethargy especially aggregated on bending forwards [8]. Characteristic physical findings are dilated, non pulsitile neck veins, increased number of collateral veins covering anterior chest wall. cyanosis, edema of face, arms and chest, proptosis, glossal and pharyngeal edema and mental obtundation. Clinical picture is mild if obstruction is located above azygous vein. Obstruction of recent onset is most likely to be of malignant in nature however long standing obstruction is usually non-malignant except SVC thrombosis. Diagnosis is clinical. Most significant chest X ray finding is widening of superior mediastinum mostly on the right side[9]. Surgery provides immediate relief for patients in whom benign process is the cause for SVC obstruction.[2]

Retrosternal goiter is the down growth of enlarged thyroid, through thoracic inlet into mediastinum and constitutes 0.2-21% of patients with cervical goiter and in 75-90% of cases it is located in the anterior mediastinum and remainder in posterior mediastinum. Mostly retrosternal goiter is part of cervical goiter, however isolated substernal goiter has been described in literature.[10] Complications of cervical goiter like thyrotoxicosis and malignancy also occur in it. Retrosternal goiter causes pleural effusion in 25% of cases, however if other characteristic findings are present, a diagnosis of SVC is still possible in presence of normal chest x ray. C.T. provides most reliable view of mediastnal anatomy i.e.; diminished or absent opacification of central venous structures with prominent collateral venous circulation. MRI has no advantage over CT and invasive procedure like Broncoscopy and PCNB – mediadstonoscopy even thoracotomy can be performed. If patient has known malignancy, detailed workup is not necessary and usually appropriate treatment may be started after obtaining CT scan of the thorax. However for those with no history of malignancy, a detailed evaluation is absolutely necessary to rule out benign causes and also for tissue diagnose to direct appropriate therapy even before initiation of glucocorticoids and radiation. [1]. Treatment of SVC'S includes head elevation, oxygen, emergent therapy in case of tracheal obstruction; diuretics with low salt diet, radiation therapy is the primary treatment for SVC'S by non-small cell lung cancer and other metastatic a significa nt potential for tracheal deviation or obstruction beca use of limited space for expansion of goiter [1,2]. Retrosternal goiter presents as SVC syndrome with resulting dilated cervical and facial veins. Some present with symptomatic mediastinal mass on chest X ray. Treatment of retrosternal goiter is resection unless contraindication are present because it never regresses with thyroid hormone treatment and tracheal compression can lead to serious respiratory embracement [2].

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TUBERCULOUS OSTEOMYELITIS INVOILVNG RARE SITES

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Abstract: Two cases of sternal and one of matacarpal tuberculous osteomylitis are presented in this study as both the sites are rarely involved in tuberculosis. All of them presented clinically with swelling of effected part with draining sinus in two cases and vague symptoms like weakness, loss of appetitiei and lack of drive in all of them. FNAC smears confirmed diagnosis in two cases of sternal tuberculosis in which AFB was isolated and Gopsy in one case (Metacarpal) in which isolation of AFB was not attempted. All responded to ATT well.

Key words: Metacarpal, Osteomylitis, sternum, tuberculosis.

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Introduction

Tuberculosis of sternum and small bones of hand is very rare[1,2]. Only six cases of tuberculous osteomytitis of sternum were reported up to 1985 from India[1]. Since then more cases have appeared in the literature[2]. Similarly tuberculosisi of metacarpal bones is very infrequent and earlier writers have called it spina ventosa.[1]

Case 1

A 25 year old female patient of peripheral part of Kashmir valley was referred by a physician to the diagnostic center of one of us (Dr. Chowdhary) for FNAC of swelling over sternum. The patient had low-grade fever with loss of appetite since last one month. There was no history of cough. No lymphadenopathy. The swelling located at manubrium sterni measured 3 x 2 cms, soft to cystic. Aspiration yielded thick pus, which on the microscopy smears of revealed epitheloid cell granuloma, lymphocytes and caseation necrosis. Z. N. Staining demonstrated Acid Fast Bacilli in the smears which confirmed the diagnosis of tuberculosis X-ray chest did not show any pulmonary lesion. Sternum revealed lytic lesion with erosion of the cortex

Case 2

A 60 year old female from rural Kashmir who looked weak, emaciated was advised cytological examination of the contents of draining sinus over the sternum. The exfolative cyitology showed pus cells with necrotic debris only. Aspiration cytology from the peripheral part of swollen area showed the presence of epitheloid cell granuloma with giant cells, caseation necrosis, pus cells and fibroblasts. Z.N. Staining showed the presence of Acid Fast Bacilli

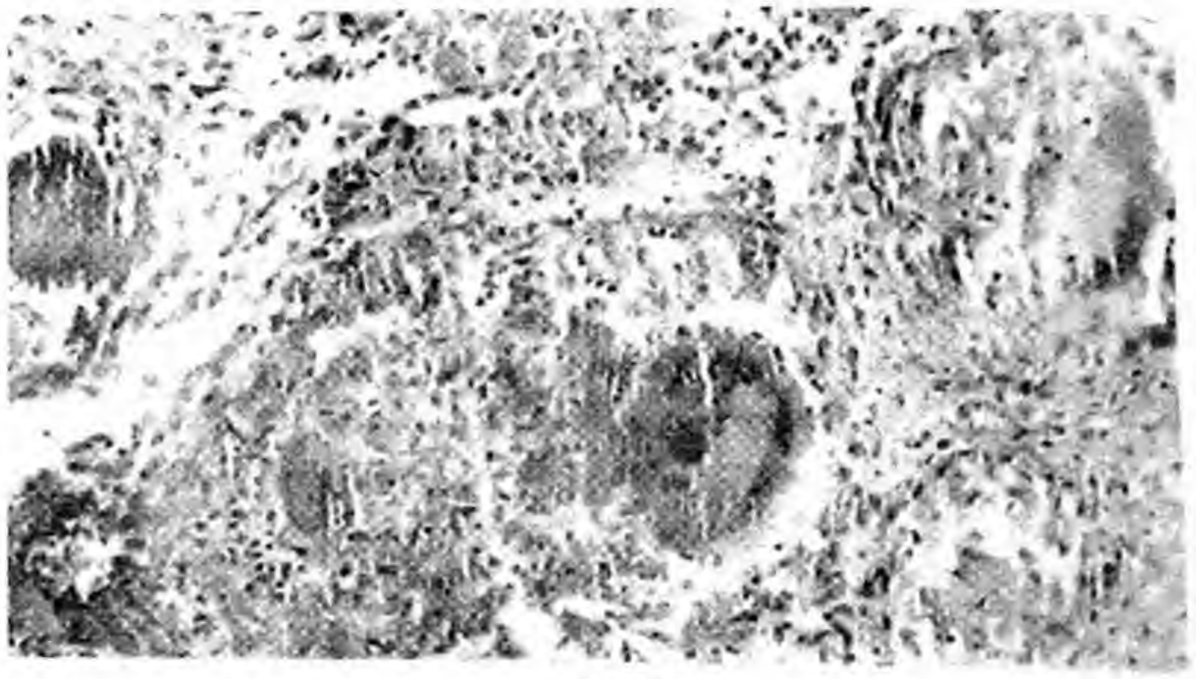

Fig 1:

and diagnosis of tuberculous osteomylitis was confirmed X-ray photograph taken earlier had shown lytic lesion of bone underlying the swollen part. Other significant hematological investigation included high ESR with lymphocytosis.

Case 3

A 14 -year old patient developed painful swelling and draining sinus on right hand apparently following trauma. X-ray revealed multiple fractures of the small bones of hand, open biopsy taken showed epitheloid cell granulomas, abundant Langhan's type of giant cells (Fig 1) with caseation necrosis. The diagnosis of tuberculous osteomylitis was confirmed.

Discussion

Tuberculous osteomylitis in comparison to pyogenic osteomylitis is rare in industrialized nations. In developinig

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countries, however, tuberculous osteomylitis is still a great problem to deal with. In developed countries it affects old, Immune-compromised patients whereas in the poor countries the patients are young adults or adolescents.[4] Mostly tuberculous ostiomylitis is secondary to the dissemination of mycobactarium tuberculosis from primary sites else where in the body, most commonly, pulmonary, gastrointestinal or renal foci or local extension from tuberculous arthritis[2-5]. Sternal tuberculosis in majority of cases is secondary to pulmonary tuberculoses or tuberculous lymphadinitis. Since 1985 sternal tuberculosis has been reported in association with spontaneous fracture of sternum[1], in case, of disseminated tuberculosis, thalassemia and post coronary bypass surgery[1,6,7].

Ernest Aegerter et al[2] recorded only one case of multiple tuberculous infection of metacarpal bones, a condition that earlier writers called spina ventosa. Infection of entire shaft of one bone or more of short cylindrical bones occurs with expansion of shafts by subperiosteal apposition. We observed a similar case with multiple fractures of multiple metacarpal bones, abscess formation leading ito draining sinus. The pattern of tuberculous osteomylitis seems changing. The vertebral Kock was thought to be the commonest sites of the bone involvement in tuberculosis (50-60%) but its incidence seems to be decreasing and rare bony involvement such as scapula, acromion and tarsal bone has shown increasing incidence.[5]

All of our cases were put on Antitubercular 4-drug therapy for first two months, followed by two-drug combination for 4 months. All showed excellent response.

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DUODENAL TUBERCULOSIS

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ABSTRACT: *Pasteurization of milk and effective treatment of tuberculosis have greatly reduced the incidence of upper gastrointestinal tuberculosis. When it does occur, it is commonly mistaken for peptic ulcer disease, Crohn's disease or neoplasm , both clinically and radiologically. This paper reports a case of isolated duodenal tuberculosis ; a very rare entity.*

Key words: *Tuberculosis, Duodenum, Gastrointestinal tract.*

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Case Report

A 25 years old male presented with the complaints of epigastric pain and occasional postprandial vomiting of six months duration. His physical examination was unremarkable. Laboratory investigations revealed hemoglobin of 13.5gm%, WBC count of 12,800 with normal differential and blood chemistry within normal limits. Chest X-ray was normal. He underwent a Barium meal study which revealed mucosal irregularity and narrowing of the second part of duodenum. (Fig. 1). The patient was treated for peptic ulcer disease but the pain persisted. Sonography done 3 months later revealed few hypoechoic nodes near the pancreatic head. Barium meal follow through study was unremarkable. Endoscopy showed mild antral gastritis, mild inflammation of the duodenal bulb and severe postbulbar stricture. Biopsy showed chronic duodenitis.

Fig 1: Double contrast Barium meal study showing long stricture involving the second part of duodenum. Stomach and duodenal cap are normal.

The gastroenterologist felt that ulcer disease was unlikely in view of lack of response to ulcer treatment. Crohn's disease was also unlikely in view of normal small bowel series. As the pain persisted and sonography showed few nodes near pancreatic head, the patient underwent exploratory laparotomy. At surgery, the duodenum was markedly inflamed from pylorus to distal portion and second portion was stenotic. The stomach, jejunum and ileum were normal. Few small nodes were seen in the mesentery and near the pancreatic head. A gastrojejunostomy was performed. Biopsy from duodenum and lymph nodes revealed hyperplasia and tubercles with caseation surrounded by epithelioid cells and some Langhans giant cells. The patient was put on antitubercular therapy but was subsequently lost to follow up.

DISCUSSION

Gastrointestinal tuberculosis is not an uncommon entity in the developing countries .It usually occurs in patients with pre-existing pulmonary tuberculosis[1]. In the presence of untreated T.B, the incidence of G.I.T involvement is relatively high. By far the most common site of G.I.T involvement is the ileocecal region ; the ascending colon and jejunum are next common sites. The stomach, duodenum, distal colon and oesophagus are rarely involved. Good[2] found the average incidence of gastric T.B in

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autopsies and gastric resections from Mayo Clinic and other published figures to be 0.34%.If only the cases with other T.B were considered, the incidence rose to 1.4%. Isolated duodenal T.B is a rare occurrence, an incidence of less than 3% is reported in most series[3].

The extreme rarity of gastric and duodenal T.B in patient's with pulmonary or intestinal T.B led many authors to postulate several factors for this rare localization. These have been:[1] sparsity of lymphoid structures in the gastric wall[2] intact gastric mucosa[3] acidity of the stomach[4] rapid passage of the ingested organism through stomach and duodenum. The possible routes of infection that have been considered include:[1] direct infection through mucosa[2] hematogenous spread[3] lymphatic spread[4] spread from serosa by continuity from adjacent structures, especially the lymph nodes.

Duodenal T.B may be asymptomatic or give symptoms and signs identical with those of duodenal peptic ulcer with obstruction. In 50% patients , there is a palpable mass. Hypochlorhydria and achlorhydria are frequent abnormalities. The radiological abnormalities_may be classified as predominantly ulcerative and predominantly hyperplastic type4. When ulcers occur, they are frequently small, superficial and multiple and appear radiologically as spiculations Long narrow ulcers situated between hyperplastic folds may be produced and may resemble ulcers of Crohn's disease. Obstruction of the lymphatics may lead to edematous coarsening of mucosal folds and a malabsorption pattern[3]. Fibrosis is very common and frequently results in strictures of second part of duodenum, as was also seen in our case. When the adjacent lymph nodes are large , the resultant extrinsic mass may indent the duodenum. .Caseation of nodes can lead to fistula formation and development of sinus tracts. Simultaneous involvement of stomach and duodenum increases the possibility of tubercular etiology although it may occur in carcinoma and lymphoma also.

To conclude, there are several features like lack of response to treatment, hypochlorhydria / achlorhydria and radiological findings of simultaneous involvement of stomach and duodenum, presence of fistulae or sinuses and signs of external pressure by enlarged lymph nodes that should make one consider the possibility of T.B, even in absence of any pulmonary lesion.

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MALIGNANT MEGAKARYOCYTOSIS

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Abstract: *Malignant Megakaryocytosis is an uncommonly recognized disorder that is characterized by rapidly progressive proliferation of atypical megakaryocytes and their percussor cells. It icomprises about 5-10% of acute myeloid leukemia and platelet count may be normal or increased. its incidence is 4.6 iper lac population. It has been diagnosed first time in our hospital.*

Key words: *Megakaryocytes, malignant, leukemia*

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Case Report

A 55 years old male painter was admitted in a medcal ward of S.M.H.S. Hospital with the history of exertional breathlessness, easy fatigability for last two years, loss of appetite, burning sensation of feet and hands, loss of weight, night sweats and low grade fever since December 2000. He denied any history of bleeding from any site or bowel and bladder disturbances. There was no history suggestive of hypertension, diabetes mellitus or tuberculosis.

Clnical examination revealed pulse: 96 bpm, BP: 130/70, pallor with no jaundice, cyanosis, lymphadenopathy, clubbing, gingival hyperplasia, lead line hyperpigmented spots, purpuric spots, ecchymotic patches, testicular or any soft tissue swelling. Chest, CNS were clinically normal. CVS revealed short systolic murmur at pulmonary area and on abdominal examination patient had hepatosplenomegaly of 3cm and 2.5cm respectively.

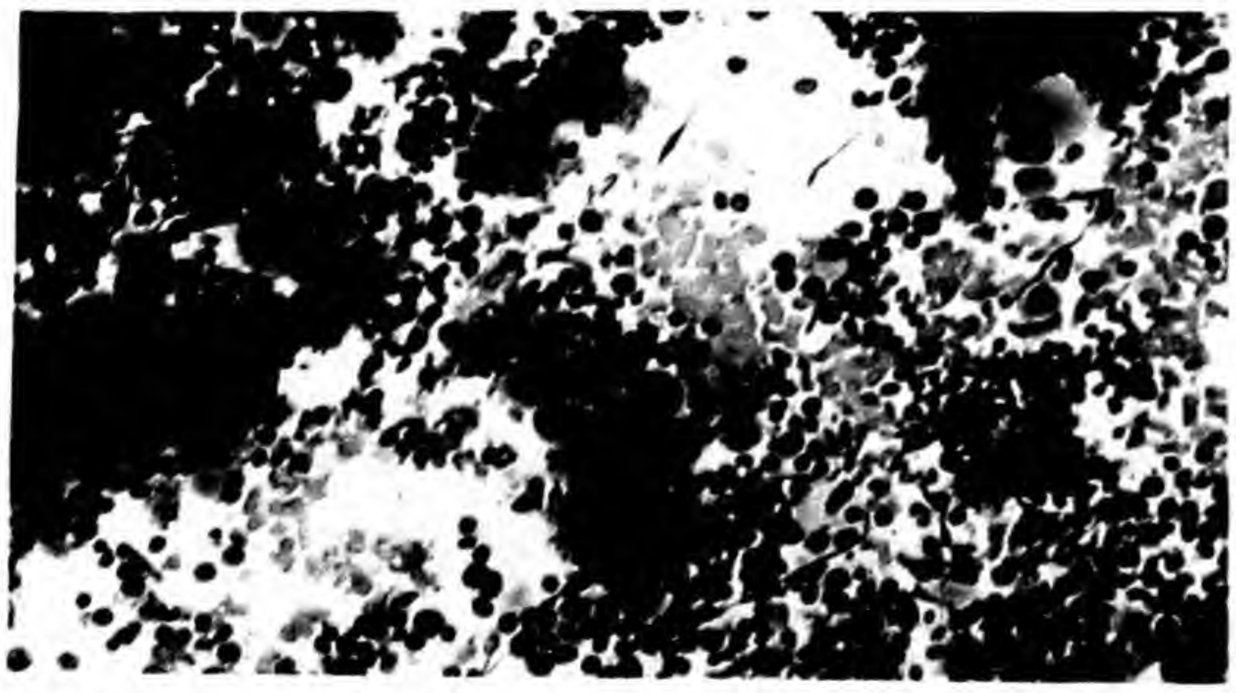

Fig-I: Bone Marrow Smear showing increased percentage of megakaryocytes and promegakaryoutes with undifferentiated blasts in the field. Leischman Stain 40x

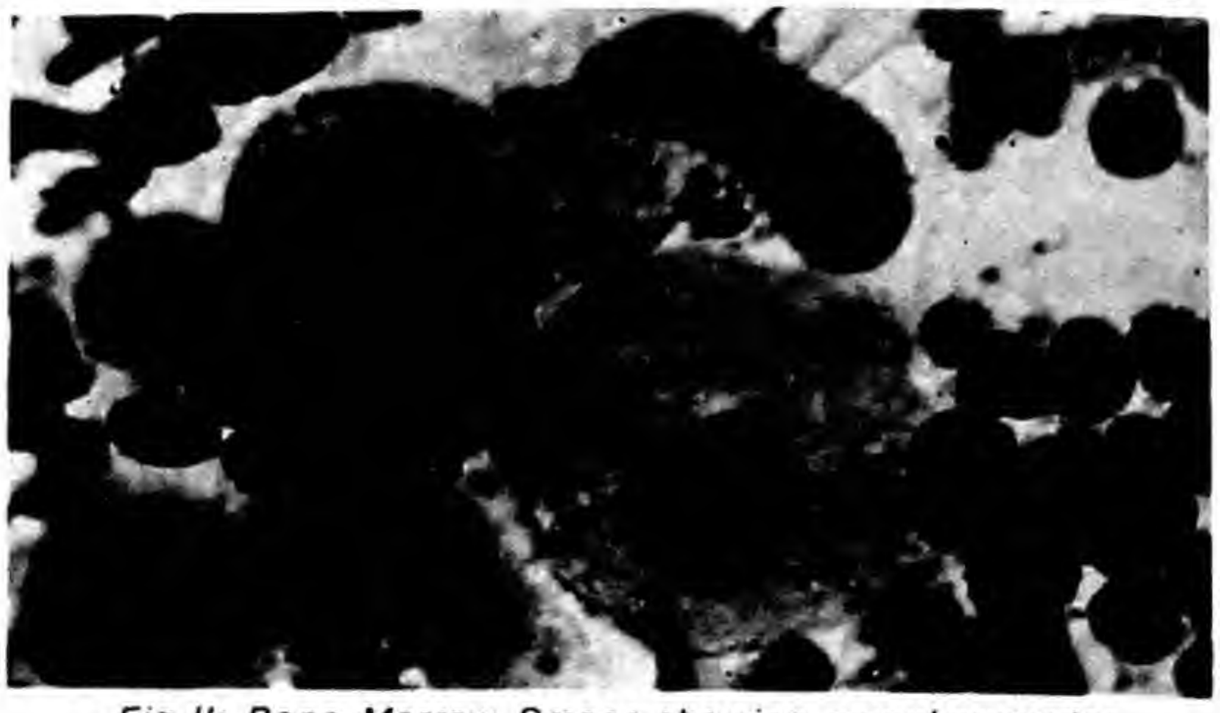

Fig-II: Bone Marrow Smear showing megakaryocytes, promegakaryoutes and undifferentiated blasts cells. Leischman Stain 100x

Routine laboratory studies were performed and showed Hemoglobin: 5.9 gm%, TLC: 5000/cm, DLC: P39L61, ESR: 45mm, BT: 1min 40 sec, C.T.: 5min 10sec. Urine examination, KFT, LFT, Blood sugars, Serum electrolytes, CXR were all normal. ECG showed RBBB, Serum iron was 66.5 ug/dl and TIBC 375ug/dl, Stool for occult blood was thrice negative, Upper GI and lower GI endoscopy revealed normal study, USG abdomen showed hepatosplenomegaly. Peripheral blood film showed marked thrombacytosis with count around 20 lac/cumm with occasional giant form of platelets and megakaryocytes at places TLC of 5000/cumm and DLC of P10L60M08E02. Red blood cells were mild to moderately hypochromic, PBF also showed fairly good number of degenerated large cells with distorted morphology.

Bone marrow aspiration done by pathologist showed

1. Hypercellular undifferentiated blasts 14-20 um with angular shape comprising of 70% marrow cell

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population.
2. Increased number of megakaryocytes along with precursor promegakaryocytes about 10% of total cell population.
3. Large primitive blasts showed cytoplasmic budding and large granules at places, blast also contain cytoplasmic vacuolations.
4. Giant blast at places.
5. Blast showed modest amount of deep blue cytoplasm.

Discussion

Malignant megakaryocytosis has been reported under several names including acute megakaryoblastic leukemia, acute megakaryocytic myelosis, acute leukemia with megakaryocytic predominance and acute megakaryocytic leukemia.[1] It was first reported by Von Boros and Koranyi in 1931 and subsequently in the American scientific literature by McDonald and hamirick in 1948.[2] It was included in FAB classificatrion in 1985 as AML-M7. (3) it is an uncommonly recognozed disorder that is characterized by rapidly progressive proliferation of atypical megakaryocytes and their percussor cells. It comprises about 5-10% of AML and incidence rate is 4.6 per lac population. It can occur at any age and sex distribution is equal. It has been linked to trisomy 21, monosomy 7, acute myelofibrosis, chronic myeloproliferative disorders, myeloid metaplasia, idiopathc preleukemia, myelodysplastic syndrome, radiation chemicals and drugs. (1) It can present as anemia, neutropenia, bleeding disorders, fever, night sweats, organomegaly, weight loss, bone pains and osteosclerotic and osteolytic lesions. Fever can occur in absence of infection and bleeding in absence of thrombocytopenia. Bleeding occurs due to deficiency of factor V.

1. Morphological features of blasts which shows size of 10-40um, angular cells with 5-6 nuceli, high nuclear cytoplasmic ratio, cytoplasmic budding, cytoplasmic granules, basophilic cytoplasm round or lobulated nuclei, cytoplasmic blebs, acidophilic nuclear chromatin with finely dispersed strands.
2. Cyrtochemical stains are usually negative Auer rods, myeloperoxides sudan black B, chloroacetate esterase and toluidine blue. Lukemic cells demonstrate diffuse acidic phosphate activity. There can be occasional PAS positivity.
3. Immunophenotyping is usually positive for factor VIII related antigen CD13, CD33, CD41a (GP IIb/IIIa), CD2b (GP Ib) and CD61 (GP IIIa).
4. Electron microscope platelet peroxidase reaction is most sensitive and specific for AML-M7. Perinuclear cisternae and endoplasmic reticulum.
5. Cytogenetic markers which will show absence of chromosome 17 and Y, monosomy of chromosomes 2, 5, 7, 16 and 21 (in infants), t(1.21) in children.

Therapy is usually directed towards:

A) Supportive care which comprises blood transfusion, hyuration, allopurinol, antibiotics and leukapheresis.

B) Definitive treatment:

The main aim of definitive treatment is remission induction Remission induced therapy comprises:

1. Cytarabine, Doxorubicin.
2. DAT regime:
   Doxorubicin, Cytarbine, Thioguanine.
3. Idarubicin, cytarabine
4. High dose Cytarabine, Asparaginase.
5. High dose Cytarabine, Doxorubicin
6. Etoposide

C) Bone marrow transplantation:

Indication:-
Age less than 60 years.
Relapse
After first remission
Refractory leukemia

The results of conventional chemotherapy of acute megakaryocytic leukemia have generally been disappointed.

Our patient was having clinical presentation compatible with acute megakaryocytic leukemia which comprises of

1. History of chemical exposure (painter).
2. PBF shows thrombocytosis
3. Undifferentiated blasts of 10-14 um size with 70% marrow population. Primitive blasts with cytoplasmic budding and large grnules at places. Cytoplasm contains vacuolation and blast contains deep blue cytoplasm.

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HEPATITIS B: GLOBAL EPIDEMIOLOGY, CONTROL STRATEGY AND VACCINATION
RELEVANCE OF THESE MEASURES AND UNIVERSAL VACCINATION IN KASHMIR.
A PERSONAL PERSPECTIVE

Mohd Sultan Khuroo MD, DM, FRCP(Edin.), MACP

During my recent visit, many doctors and public figures confronted me about my views regarding recent Hepatitis B vaccination drive in the Valley. It was not possible for me to give a simple answer, as it is a complex subject.

This report on hepatitis B epidemiology, control measures and status on vaccination (globally, in India and in Kashmir) should be seen as an answer to these questions and as information to health care planners and local experts who may like to use the data included. These data are taken from international publications and guidelines. Data on hepatitis B status in Kashmir have been drawn from data, which I have collected and published over last 30 years during my work in the Valley.

Vaccination has been the most cost effective way to control many diseases in the community globally and we have been able to eradicate small pox from the globe and are on the brink of becoming poliomyelitis free in the near future. Diseases like Diphtheria, Tetanus, Measles and Whooping cough have been controlled to a large extent in areas where "EPI" (Extended Program for Immunization) has been successful.

Hepatitis B vaccination in a community has to be seen from following angles, which are debated and discussed in this report:

1. Load of infection and consequent disease in the community (priority status)
2. Mode of transmission of disease
3. Age of occurrence of disease and probability (rate) of its becoming chronic
4. Best way to control hepatitis B in a community- other than vaccination
5. Role of vaccination- selected (high risk groups) and universal; it's immediate and long term effects; costs involved; strategy to attain vaccination targets; monitoring of vaccination and studying impact of vaccination on the hepatitis B epidemiology.

At the end I shall give my humble opinion about control of hepatitis B in Kashmir dependant upon above.

Viral hepatitis

Viral hepatitis is a global public health problem. Five major agents cause viral hepatitis namely:

1. Hepatitis A virus
2. Hepatitis B virus
3. Hepatitis C virus
4. Hepatitis D virus
5. Hepatitis E virus

To get first hand information on the global impact of viral hepatitis on human health, I have reviewed the subject in the recent past and would like you to study this document (Khuroo el al Viral Hepatitis- A personal Perspective. JK Practitioner 2000; 7: 4-11).

Hepatitis B

Hepatitis B virus belongs to the family of hepadnaviruses, which include duck hepatitis virus, woodchuck hepatitis virus, and ground squirrel hepatitis virus.

The complete virion is 42 nm in diameter.

It consists of:

1. an envelope composed of surface protein (Hepatitis B virus surface antigen- HBsAg),
2. a soluble antigen covering inside of envelope (Hepatitis B virus e antigen-HBeAg)
3. A central core containing
   a. Core protein (Hepatitis B virus Core protein-HBcAg),
   b. The viral genome known as hepatitis B virus DNA (HBV DNA),
   c. The polymerase protein for replication of DNA called the hepatitis B virus DNA polymerase (HBV DNA polymerase).

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The spectrum of clinical manifestations of HBV infection include following:

1. Acute infection called acute hepatitis B: Acute hepatitis B presents in one of the following ways:
   a. Sub clinical hepatitis (person has no symptoms about the infection)- commonest mode of presentation- 70 percent
   b. Icteric hepatitis (patient develops jaundice which lasts for 4-6 weeks)-unusual mode of presentation- 30 percent
   c. Fulminant hepatitis (patient develops liver failure and coma and can die)- rare mode of presentation- 0.1-0.5 percent.
2. Chronic infection: This presents as one of the following ways:
   a. Hepatitis B carrier: person carries virus in the liver and blood but otherwise healthy and develops no problems – commonest mode of presentation for chronic infection-. Long-term follow-up studies of hepatitis B carriers have shown that the majority remain asymptomatic with a very low risk of liver disease.
   b. Chronic hepatitis B: person carries virus in the blood and develops inflammation in the liver. Usual symptoms are vague ill health, fatigue and episodes of jaundice. - Unusual mode of presentation. If not treated he may develop permanent damage to liver called cirrhosis.
   c. Cirrhosis of liver: chronic hepatitis B is one of the many causes of cirrhosis of liver.
   d. Liver cancer: Chronic infection with hepatitis B and cirrhosis together cause liver cancer after 20 to 40 years of infection. Hepatitis B infection with liver cirrhosis is one of the important causes of liver cancer.

The clinical outcome of HBV infection depends upon the age at infection, the level of HBV replication, and the immune status of the host.

Hepatitis B infection- Epidemiology

Global impact

Hepatitis B virus (HBV) infection is a global public health problem. It is estimated there are 300 million HBV carriers in the world. These carriers are carrying the virus in the liver and blood and have low risk of developing disease in their life- time. Of the 300 million persons carrying the virus, about 250,000 (one in 1200) can develop disease and die annually from HBV-related liver disease.

However these subjects can transmit infection to others by number of known ways: neonates (perinatal transmission by pregnant mothers), from child to child (horizontal transmission during early school life), to others through percutaneous route (blood transfusions, sharing needles-illicit drug abusers or through practice of use of un-sterile needles or medical instruments) and sexual contact (homosexual and promiscuous heterosexual practice).

Transmission

Hepatitis B infection is transmitted in following 4 ways:

1. Perinatal transmission: Transmission takes place at the time of delivery by maternal-fetal transfusion and exposure to maternal blood in the birth canal, and postnatally through close mother-baby contact. Transplacental passage of HBV is very rare.
2. Horizontal transmission: Children acquire HBV infection through horizontal transmission via minor breaks in the skin or mucous membranes or close bodily contacts with other children. This infection occurs at ages between 5 to 7 years when children start schooling.
3. Sexual transmission: Homosexual behavior and promiscuous heterosexual behavior with change of multiple partners can transmit hepatitis B infection.
4. Percutaneous transmission: Hepatitis B infection can be transmitted by extremely small quantities of infected blood (less than 0.0009 ml). Percutaneous transmission can occur in following circumstances:
   a. Unsafe blood transfusions: blood from healthy hepatitis B carrier is a potential and important cause of hepatitis B which can be controlled by testing blood prior to its use. Paid blood transfusion is of particular risk in transmitting hepatitis B.
   b. Sharing of needles by drug abusers is a common cause of hepatitis B
   c. Unsterile needle and medical instruments: Hepatitis B can be transmitted through use of unsterile needles and medical instruments by dentists, medical instruments for medical examination and invasive procedures like endoscopies. Boiling of the instruments does not prevent this transmission. Instruments should be either sterile or single use (disposable).
   d. Nosocomial transmission: HBV is the most commonly transmitted blood-borne virus in the healthcare setting. Transmission generally occurs from patient to patient or from patient to health care personnel via contaminated instruments or accidental needle stick. Healthcare workers, particularly surgeons, pathologists, and physicians working in hemodialysis and oncology units, have the highest risks of HBV infection. In comparison, transmission of HBV infection from healthcare workers to patients is rare. Healthcare workers who are chronic hepatitis B carriers and are HBeAg positive are a potential risk to transmit disease to their patients particularly if they perform invasive procedures.

Chronicity

Chronicity of hepatitis B (probability of acute hepatitis B becoming chronic hepatitis B virus infection)

Probability that acute infection shall become chronic hepatitis B virus infection is exclusively dependant upon the age at which the hepatitis B infection occurs. Three patterns are seen:

1. Neonatal infection (perinatal transmission): The rate of progression from acute to chronic HBV infection is approximately 90 percent for perinatally acquired infection.
2. Childhood infection (Horizontal transmission): 20 to 50 percent for acute infections between the age of 1 and 5 years become chronic.
3. Adult infections (percutaneous and sexual transmission): less than 5 percent for adult-acquired infection become chronic.

Carrier rate (zonal distribution of hepatitis B in the world)

The impact of hepatitis B virus infection is estimated by the carrier rate in the population. This carrier rate has wide variation, but can broadly be divided into three groups:

1. High endemic zone: carrier rate of 10 to 20 percent.
2. Intermediate endemic zone: carrier rate of 3 to 7 percent
3. Low endemic zone: carrier rate of 0.1 to 2 percent.

It is most essential to understand that three zones of the world differ from each other by: 1) zones of occurrence, 2) carrier rate, 3) mode of transmission, 4) age at which acute infection occurs, 5) manifestations of acute infection, 6) chronicity (probability of acute infection becoming chronic), 7) duration of infection in the community, 8) incidence of cirrhosis & liver cancer in the population, 9) impact of disease in the health care planning and 10) best control mechanism for the infection 11) country which has adopted this model of control.

High endemic zone.

1. Zones of occurrence: southeast Asia, China, sub-Saharan Africa
2. Carrier rate: 10 to 20 percent
3. Mode of transmission: exclusively perinatal
4. Age of acute infection: neonatal life, first month of life.
5. Manifestations of acute infection: all infections are subclinical, no symptoms occur with this infection.
6. Chronicity: 90 percent of infections become chronic
7. Duration of infection in the community: as infections occur in first month of life, infections are of prolonged duration in this population.
8. Incidence of liver cancer: Incidence of liver cancer in this population is over 100 per 100,000 per year.
9. Impact of disease: Hepatitis B is a number one killer disease in this population by cirrhosis and liver cancer. Health care planners in this region have defined control of hepatitis B as number one priority.
10. Best control mechanism: Universal vaccination at birth and block transmission of disease.
11. Country, which has adopted this model: classical example Taiwan, universal vaccination in this model is extremely cost effective.

Intermediate endemic zone

1. Zones of occurrence: Mediterranean countries, Japan, Central Asia, Middle East, and Latin and South America
2. Carrier rate: 3 to 7 percent
3. Mode of transmission: exclusively horizontal
4. Age of acute infection: preschool and early school age
5. Manifestations of acute infection: all infections are subclinical, no symptoms occur with this infection.
6. Chronicity: 30-50 percent of infections become chronic
7. Duration of infection in the community: as infections occur in first few years of life, infections are of prolonged duration in this population.
8. Incidence of liver cancer: Incidence of liver cancer in this population is around 40 per 100,000 per year.
9. Impact of disease: Hepatitis B is an important killer disease in this population by cirrhosis and liver cancer. Health care planners in this region have defined control of hepatitis B as important priority.
10. Best control mechanism: Universal vaccination at birth and catch up vaccination in the preschool period blocks transmission of disease, which occurs at preschool and school age.
11. Country, which has adopted this model: classical example Saudi Arabia. Universal vaccination in this model is extremely cost effective health care policy.

Low endemic zone

1. Zones of occurrence: North America, Western Europe, Australia and New Zealand
2. Carrier rate: 0.1 –2.0 percent
3. Mode of transmission: exclusively percutaneous or sexual (see details below)
4. Age of acute infection: adult life (20 to 40 years)
5. Manifestations of acute infection: about 30 percent infections are symptomatic and cause icteric hepatitis, 0.1 to 0.5 percent present with fulminant hepatitis.
6. Chronicity: less than five percent of infections become chronic
7. Duration of infection in the community: as infections occur in adult life, infections are of short duration in this population.
8. Incidence of liver cancer: Incidence of liver cancer in this population is from 0.1 to 4 per 100,000 per year.
9. Impact of disease: Hepatitis B is not an important disease in this population as compared to other two

zones. Health care planners in this region have defined other important diseases as priority for control.

10. Best control mechanism: best way to control hepatitis B in this community is to prevent percutaneous transmission and sexual transmission. This is to be done by safe blood, good medical practices, and control of illicit drug abuse. In addition vaccination for high-risk groups is important way to reduce hepatitis B transmission. Vaccination for general population, which are low risk to hepatitis B, has to be seen from cost effective point of view, general economical situation of the country and health priorities of the community. In countries with low endemicity, the benefits of universal neonatal vaccination will not be apparent until two to three decades later because infection in these countries usually occur among adolescents and young adults through percutaneous or sexual routes.
11. Country which has adopted this model: all developed countries have developed strict measures to control hepatitis B by safe blood, safe medical practices, mass population awareness and vaccination for high risk groups. Except United States, none of the developed countries have yet taken up mass vaccination program (hepatitis B status in USA needs a special discussion and has been done in pages to follow). For example countries like United Kingdom and Scandinavian countries with very strict health care policies and with good health care budgets have not used universal vaccination policy.

Hepatitis B in USA
(mixed epidemiological status due to inhomogenous and ethnically variable population)

1. Zone of occurrence: United States of America
2. Carrier rate: USA is a multiethnic society, carrier rate is 0.1 –0.5 percent in whites, however, specific ethnic groups residing in the US namely Alaskan Eskimos, Pacific Islanders, Hispanics, black Americans and first generation immigrants from high endemic zones namely mainland China, the Philippines, Vietnam, Korea and Japan have chronic carrier rate of 5 to 15 percent.
3. Mode of transmission: variable; dominant source of transmission is sexual (homosexual and promiscuous heterosexual practice) and illicit drug use with needle sharing in drug abusers; however, in populations like Alaskan Eskimos, Pacific Islanders, Hispanics, black Americans and first generation immigrants from high endemic zones namely mainland China, the Philippines, Vietnam, Korea and Japan perinatal transmission is common
4. Age of acquisition of infection: majority of infections occur in adults, however, Alaskan Eskimos, Pacific Islanders, black Americans and first generation immigrants from high endemic zones namely mainland China, the Philippines, Vietnam, Korea and Japan develop infections in childhood.
5. Manifestations of acute infection: 30 percent of adult infections are symptomatic, while, 70 percent are subclinical. However, infections on children are asymptomatic.
6. Chronicity: Five percent adult infections become chronic, while, 20 to 90 childhood infections become chronic.
7. Duration of infections: As most of infections are of adult onset, duration of infection is short lasting.
8. Impact of disease to the community: 1.25 millions are chronic carriers and 5000 deaths as a result of chronic liver disease per year.
9. Incidence of liver cancer:
10. Hepatitis B control measures: control of hepatitis B in USA has passed through many phases and the impact of each control policy is well studied:
    a. Safe blood, excellent safe medical practices, result of safe sexual practices and vaccination of high risk groups reduced impact of hepatitis B infection. Estimated incidence of acute hepatitis B infection reduced from 70 per 100,000 per year in 1985 to 40 per 100,000 per year in 1991. However, majority of this impact of reduction of hepatitis B load was related to safe practices rather than vaccination for high-risk groups. Failure of vaccination of high risk groups to effect the epidemiology of hepatitis B occurred in this community because of number of reasons: i) only 10 percent of high risk groups could be targeted, this was due to difficulty in identifying high risk groups and lack of compliance of this population to vaccination (illicit drug users and homosexuals), ii) 30 percent of acute sporadic infections occurred in low risk groups which were not targeted, iii) a large pool of population with high endemicity of hepatitis B was not targeted for control
    b. In 1991, Centre for Disease Control (CDC USA) recommended universal vaccination for all neonates. This was done as vaccination for high-risk groups had failed in this community for reasons above. It was felt that it would take 20 to 30 years for this program to show results as most of the infections occur in adults.
    c. In 1994, CDC USA expanded the recommendation to include all 11 and 12 year-old children who had not been previously vaccinated and all less than 11 years children from high risk groups of hepatitis B infection (Alaskan Eskimos, Pacific Islanders, Hispanics, black Americans and first generation immigrants from high endemic zones namely mainland China, the Philippines, Vietnam, Korea

and Japan). This was done to accelerate the decline of incidence of hepatitis B and reduce the time factor of 20 to 30 years to reduce impact of hepatitis B infections. Recently CDC USA has recommended extending the vaccination to all children between 0 to 18 years of age. This shall further accelerate the decline of incidence of hepatitis B.

Hepatitis B in India (mixed epidemiological status)

1. Zones of occurrence: India
2. Carrier rate: 2 to 3 (2.5) percent
3. Mode of transmission: mixed; predominantly percutaneous route, perinatal transmission is rare (less than 5 percent), horizontal transmission may possibly contribute to less than one fifth of hepatitis B carriers.
4. Age of acute infection: adult life (20 to 40 years)
5. Manifestations of acute infection: about 30 percent infections are symptomatic and cause icteric hepatitis, 0.1 to 0.5 percent present with fulminant hepatitis.
6. Chronicity: less than five percent of infections become chronic
7. Duration of infection in the community: as infections occur in adult life, infections are of short duration in this population.
8. Impact of disease: Based on above data with population of India of one billion, 40 million hepatitis B carriers exist in India. Of these around 36 million will stay as asymptomatic carriers and shall never develop any disease. Around 4 million shall develop chronic hepatitis and cirrhosis and three hundred thousand (300,000) cases of liver cancer shall occur per year.
9. Incidence of liver cancer: Incidence of liver cancer in this population is between 1 to 4 (overall around 3) per 100,000 per year.
10. Best control mechanism: Unsafe blood is rampant, unsafe medical practices are common, no regular program for high risk groups exists and none of the states can offer neonatal vaccination program because of health care priorities and budgetary constraints. A massive program nationwide is needed for basic health care policies to reduce hepatitis B spread and should focus on safe blood and safe use of needles and medical instruments. A public health program to reduce illicit drug abuse is important. Vaccination for high-risk groups is cost effective. Once basic health policies are Targeted, mass vaccination program can be undertaken if budgetary constraints are removed.

Hepatitis B in Kashmir

(distinct epidemiology due geographically and ethnically homogeneous population)

Overall the last 30 years I have studied the epidemiology of all five hepatitis viruses in the Valley and have been published in over 26 publications. A lot of data has accumulated in the form of postgraduate and postdoctoral dissertations and thesis and some has stayed unpublished. Taking strength from these publications and observations, hepatitis B epidemiology in Kashmir has following characteristics:

1. Zone of occurrence: Kashmir (Jammu & Ladakh may have similar epidemiology but have not been studied in any detail)
2. Carrier rate: less than 2.0 percent (around 1.5 percent)
3. Mode of transmission: exclusively percutaneous (unsafe blood and unsafe medical practices like use of unsterile needles, unsterile medical appliances for common practices like dental check up and work, tattooing, acupuncture etc.
4. Age of acute infection: adult life (20 to 40 years)
5. Manifestations of acute infection: about 30 percent infections are symptomatic and cause icteric hepatitis, 0.1 to 0.5 percent present with fulminant hepatitis
6. Chronicity: less than five percent of infections become chronic
7. Duration of infection in the community: as infections occur in adult life, infections are of short duration in this population.
8. Impact of disease: An estimated 50,000 (fifty thousand) hepatitis B carriers exist in valley. Most of these carriers are asymptomatic and shall never get ill. In view of low prevalence of chronic alcoholism, progression of hepatitis B carrier state to chronic hepatitis and cirrhosis is slower and less common than those places where such habits are accepted by the society. My estimate is that we have around 5,000 persons with chronic hepatitis in the valley at any one time. Not more than 50 patients with end stage liver disease and around a dozen cases of liver cancer occur in the Valley per year.
9. Incidence of liver cancer: Incidence of liver cancer in this population is less than 1 per 100,000 per year. Less than a dozen primary liver cancers are reported from Kashmir per year.
10. Best control mechanism: best way to control hepatitis B in this community is to start a long-term health care plan. First and foremost we must use fundamental medical practices to prevent percutaneous transmission. This is to be done by safe blood, good medical practices especially in dental clinics, control of reuse of unsterile needles and mass awareness program about hepatitis B spread and control. In addition vaccination for high-risk groups is important way to reduce hepatitis B transmission and is a must.

We might debate why bother about these practices at all and why not vaccinate every body (universal vaccination). This is wrong practice because of

following reasons:

i) such unsafe practices spread other viruses especially hepatitis C virus and HIV. Hepatitis C virus is as or even more important cause of liver disease in the world and certainly in our community and can only be controlled by safe medical practices,

ii) even after universal vaccination, not more than 80 percent persons fully vaccinated can be protected from transmission of hepatitis B infection,

iii) even if vaccinate everybody and attain the requisite goal, it shall take a minimum of 20 to 30 years before this vaccination shall show effects. This time can be reduced to 5 to 10 years if we vaccinate all unvaccinated children from 0 to 18 years.

Vaccination for general population, which is low risk to hepatitis B, has to be seen from cost effective point of view, general economical situation of the country/ state and health priorities of the community. In Kashmir with low endemicity, the benefits of universal neonatal vaccination will not be apparent until two to three decades later because infection in these countries usually occur among adolescents and young adults through percutaneous or sexual routes. Thus, in addition to neonatal vaccination, we shall have to vaccinate preschool and school children (0 to 18 years) who are not vaccinated. We shall examine its cost effectiveness in overall context of health care plan in subsequent discussion.

11. Present model: No strict program for control of hepatitis B exists in our community. Safe blood is not available in all situations, unsafe medical practices do yet exist and have not been targeted. Till now no definite plan to follow high risk vaccination is yet available.

Hepatitis B epidemilogy, carrier rate, impact of disease to health care workers shows marked variation from country to country and from region to region in the same country like India.

Health priority before the health care workers varies depending upon health care needs and level of health care.

Eradication program for hepatitis B by universal vaccination should be seen from the point of economical situation of the State and health care pressure from the chronic hepatitis B infection.

A debate in the health care personnalle needs to done to focus the correct policies for control of hepatitis B infection in our community. Public should be informed about these discussions by data and opinions. We should not be driven by demands of drug firms; rather than our personal needs and priorities.

Hepatitis B vaccine and Vaccination Program

Hepatitis B vaccine has been a major breakthrough in control of hepatitis B infection.

Two sources of vaccines are available: i) plasma derived consisting of surface antigen particles isolated and purified from plasma of chronic infected patients, ii) Recombinant vaccines made by incorporating the surface gene of HBV into various vectors(yeast, *Escherichia coli* or mammalian cell lines). The yeast-derived vaccines are the favorite. Only recombinant vaccines are used as of today.

For normal (immunocompetant) adults, three doses at 0, one month and six months is needed. For children half dose at 0, one month and six month is needed. Dosage less than three spaced doses is useless.

Deltoid is the site for injections for adults and into lateral aspect of thigh in children.

Over 90 (80 to 95) percent shall develop protective antibodies after three spaced doses. Protection in healthy (immunocompetent) persons is lifelong and no booster dosing is needed.

Hepatitis B vaccination in patients who are immunosuppressed need different dose, dosing pattern and have low protective antibody response rate.

No need to test for hepatitis B status is needed and is not cost effective. However, if the hepatitis B carrier rate is 20 percent or above in the community, prevaccination testing by anti-HBc is cost effective. Vaccination for Hepatitis B carrier is safe and causes no harm or benefit.

Hepatitis B vaccine is safe. Isolated neurological complications (demyelinating disease) and fatalities have been linked to hepatitis B vaccine. However these outweigh the benefits of the vaccination.

Here I might add a caution and add a statement from a recent reference: "Surveillance of hepatitis B vaccine associated adverse events will continue to be an important part of hepatitis B vaccination programs even in face of current record of safety - reference- Update on viral hepatitis- AASLD(American Association for Study of Liver Diseases) postgraduate course 2000- page 90"

Post vaccination testing by effective vaccines is not necessary in healthy persons.

Indications of hepatitis B vaccine is recommended under following circumstances:

1. High risk groups: These individuals have high chance of contracting hepatitis B infection and vaccination to these individuals is highly cost effective. These are children borne to HBV carrier or infected mothers, household and sexual contacts of hepatitis B carriers or infected persons, health care workers exposed to blood, needle stick exposure to health care workers, hemodialysis patients and staff, staff of custodial institutions for the developmentally handicapped, injection drug abusers, promiscuous homosexual and heterosexual individuals, persons like hemophliacs who need long term, high volume therapy with blood products and persons traveling to endemic areas of

hepatitis B.

2. Universal Vaccination: This program envisages to immunize the whole population to prevent and finally eradicate hepatitis B virus. Three patterns of universal immunization have been practized:
   (i) Neonatal vaccination: all newborn children are vaccinated at birth. This is recommended for high incidence zones of hepatitis B, with perinatal transmission as the dominant route of transmission.
   (ii) Neonatal vaccination, with catch up vaccination for preschool children. This is done in intermediate endemic zones with horizontal mode of transmission at early school age.
   (iii) Neonatal transmission, with vaccination for all unvaccinated children from 0 to 18 years. This is recommended for low incidence zones of hepatitis B especially in USA (for details see above).

The global advisory group of the Expanded Program on Immunization (EPI) recommended integration of hepatitis B vaccine into all national immunization programs. Countries with a carrier rate of 8 percent or more were advised to commence this programs by 1995, the deadline for the other countries was 1997.

Countries that implemented universal hepatitis B vaccination programs are all high endemic zones and have begun to see the benefits. In Taiwan, vaccination of newborns of carrier mothers was implemented in July 1984 and extended to all neonates in 1986. The coverage for complete vaccination is between 84 to 94 percent. At the start of the program, the HBV carrier rates among children was 10 percent and the incidence of childhood hepatocellular carcinoma was 0.7 per 100,000 children. Ten years into the program, the HBV carrier rate among children has decreased to <1 percent and the incidence of childhood hepatocelluiar carcinoma to 0.36 per 100,000. The prevalence of anti-HBc among children >13 years old (born before the implementation of the vaccination program) also decreased from 38 percent to 10 percent. These findings demonstrated that universal vaccination can control vertical and horizontal transmission of HBV infection and the sequelae of chronic HBV infection.

In countries with low endemicity, the benefits of universal neonatal vaccination will not be apparent until two to three decades later because infection in these countries usually occur among adolescents and young adults through percutaneous or sexual routes. As explained earlier, Catch-up vaccination to children borne before universal neonatal vaccination was implemented. Most of these children are school-age. Catch-up vaccination permits these children to be immunized before they reach adolescence when they are at risk of infection through sexual exposure and intravenous drug use. The progress of catch-up vaccination in the United States has been fairly successful with over 75 percent of the parents consented, and 68 to 75 percent of the consented children completing three doses of vaccine.

For hepatitis B vaccination to be effective in its motive to bring down the impact of hepatitis B in the community, following is needed:

(i) Vaccine must be effective. It must sero-convert over 90 percent of healthy individuals after three spaced doses and give rise to protective antibody levels. This must be done by an independent group of investigators by testing a random group under vaccination program. Data studied and funded by the pharmaceutical company have conflict of interest and it is also important to test the product we are getting in the population under mass vaccination program.

(ii) Vaccination should be delivered to over 90 percent of target population to give desired results to the community. Half hearted attempts to vaccinate a small percentage of target population does not give desired results and may be harmful by making healthcare workers unduely confident of control especially in high incidence zones.

(iii) A governmental agency should own the program for legal reasons. This is of tremendous importance as is seen from the legal claims of a large groups of women who contracted hepatitis C after anti-D immunoglobulin in Scotland.

Let us now look at what are our options for control of hepatitis B in Kashmir. This should be seen under following heads:

(i) Is hepatitis B our high health care priority: No. Infections like tuberculosis, diarrheal diseases, parasitic diseases, hepatitis E and cancers of food pipe and stomach, peptic ulcer etc are major killers. Hepatitis B, fortunately, has a much less impact in our community.

(ii) How to control hepatitis B in Kashmir: First thing is first. We must put every effort to improve our medical practices to a respectable level of safety. This includes use of safe blood and blood products, to ban use of unsterile needles and medical equipment in all official and unofficial situations and improve infection control policies in hospitals and clinics.

(iii) Allow hepatitis B vaccine for high risk group in our community.

(iv) Massive awareness program to public about infection diseases and their control including Hepatitis B.

These shall drastically reduce the impact of hepatitis B virus and also other more important infections like hepatitis

C virus and AIDS.

Role of universal vaccination program in Kashmir.

This needs to be seen from following points:

(i) Costs involved: At a cost of Rs.100 per adult dose and Rs.50 for pediatric dose, estimated cost of adult vaccination is around Rs.800 for adults and Rs.400 for children (taking into account response rate of 80 percent, waste of resources due lack of compliance of completing three doses, loss of 3 or more work days in adults and logistic support from the health services). Rounding this we shall calculate at Rs.500 per vaccines.

(ii) We need to do neonatal vaccination and vaccination for all unvaccinated children from 0 to 18 years. To reach a vaccination target of over 90 percent, we need to vaccinate around half of the population (neonates and children from 0 to 18 who are not vaccinated). This shall cost around 100 crores rupees. This is a substantial proportion of our total budget and needs to be spend over a short time to start with. Over the ensuing years, budget expenditure may stay at half this amount per year.

Here I might add a paragraph which deals with expenditure of hepatitis B vaccination for high endemic zones and may be an eye opener for a low endemic zone like Kashmir:

" High cost of HBV vaccine for people in hyperendemic areas with poor economic conditions: How to reduce the cost of HBV vaccine and increase the funding for vaccination to help children of hyperendemic areas with poor economic conditions are important issues for eradication of HBV infection and its related liver complications- reference source: HEPATOLOGY IN THE NEXT MILLENNIUM: LESSONS FROM THE PAST AND ISSUES FOR THE FUTURE-NOV 1999- AASLD POST GRADUATE COURSE"

(iii) The results of this vaccination shall start showing up at least after 5 to 10 years of vaccinations as sporadic infections occur in adults.

(iv) Can we reach 90 percent target vaccination by the voluntary paid immunization program as is being practiced as of today: No. Impossible, I think we cannot reach a figure of less than 10 percent seeing the compliance of people to such paid programs, which are so widely spaced. This vaccination to be successful must be included in the EPI program.

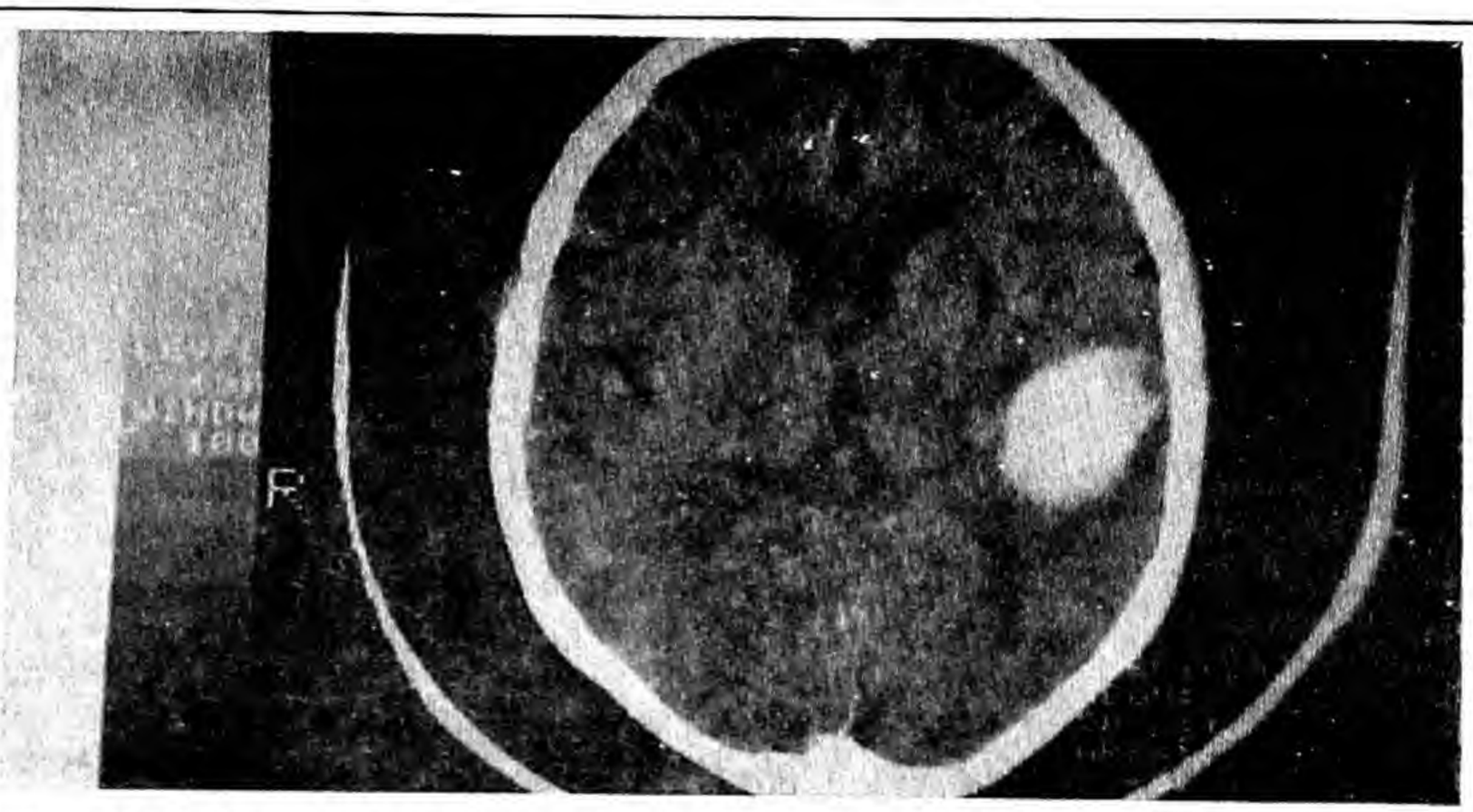
(v) Is this vaccination program being monitored for efficacy and end results: This needs baseline data by sample surveys of load of hepatitis B before and regular intervals of vaccination program. I am not sure whether baseline survey in vaccination areas has been conducted to see the impact of this program in the long run.

(vi) Will an individual who vaccinates himself or his child benefit: Answer is yes as well as no. Chances are over 80 percent that vaccines shall be protected if he gets an effective vaccine and not 100 percent: Also bad medical practices expose him to a number of hepatitis viruses and other infections.

Keeping above into account I believe we have to do public awareness, improve our safety standards and if we are planning Hepatitis B vaccination, do it correctly to attain long-term results. As a researcher in this field and as an interested party for good of those living in J&K, I shall be most happy that finally a program for control of hepatitis viruses has been started in the valley. Thank you.

The views expressed by the author are his own. We would welcome debate on the topic and are ready to publish other opinion as well.

CRACKDOWN INDUCED STROKE



60 years old female nonsmoker known hypertensive, nondiabetic presented with history of talking irrelevant immediately after hearing about the intrusion of army troops in their village for a crackdown. There was no history of headache, head trauma, unconsciousness, convulsions, incontinence of urine or feces, fever and vomiting.

On examination she had B.P. 130/80mmHg, pulse 70 bpm, bilateral carotids felt, no carotid bruit. Pupil's bilaterally equal and reacting to light. CVS revealed LV type Cardomegaly. CNS revealed sensory aphasia with no obvious motor deficit, normal deep tendon reflexes, down going planters and no signs of meningeal irritation. Rest of general and systemic examination was normal.

Laboratory studies reveled Hemoglobin: 12.6 g/dl, ESR: 14mm/hr, TLC: 8000/cumm, DLC: N80L20, Blood urea: 75mg/dl, Serum creatinine: 1.3mg/dl, Blood Sugar: 110mg/dl, Urine examination: normal, Serum Na^+: 138meq/dl, Serum K^+: 5.5meq/dl, Serum triglycerides: 250mg/dl, Serum cholesterol: 180mg/dl, LD: 180mg/dl, HDL: 55mg/dl, Total bilirubin: 0.8 mg/dl, Total protein: 5.7 g/dl, Serum albumin: 3.8 g/dl, Alkaline phosphatase: 48 units/l. ECG showed left ventricular hypertrophy, CXR: LV type cardiomegaly, Echocardiography: normal study, CT Head: Intracerebral Hemorrhage left posterior part of Sylvain fissure and parietal lobe and old infarct in right parietal lobe.

Stressful conditions as known to precipitate the vascular events coronary syndromes and strokes. Crackdown which means cordoning off and house to house search in a particular area by security forces, this puls lot of inconvenience and stress to local population for hours together. Such crackdowns are frequent in valley and people are living under tremendous stress. We attribute intracerebral hemorrhage in this patient due to crackdown.

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MELASMA - AN OVERVIEW

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Melasma is a relatively common acquired symmetric hypermelanosis characterized by irregular brown or sometimes grey-brown hypermelanosis involving sun-exposed areas.

The term melasma is derived from the Greek word "melas" meaning black and is most commonly observed in women. Chloasma is another term used sometimes to connote melasma.It is derived from the Greek word "cloazem" meaning 'to be green'. Hence this hypermelanosis should correctly be designated as melasma rather than chloasma.The true incidence of melasma is unknown. The disease affects all racial groups but is more prevalent in dark complexioned individuals (skin types IV throughVI), especially women of Hispanic descent who live in areas with intense ultraviolet radiation. Multiple factors have been implicated in the etiopathogenesis of melasma, although the precise cause is still unknown. Genetic influences, exposure to ultraviolet radiation, pregnancy, oral contraceptives, thyroid dysfunction, cosmetics,phototoxic and anticonvulsant drugs, estrogen-progesterone therapies have all been postulated as etiological agents for melasma.[1,2] However,recently imbalances in the hormonal milieu have also been implicated in the etiopathogenesis in both female as well as male patients with melasma.[3-7]

Three clinical patterns of hyperpigmentation are recognized in patients with melasma. These include a centrofacial, malar and a mandibular pattern. Based on Wood's light examination of the skin, melasma can be divided into four types. The epidermal variety is characterized by increased melanin in the basal ,suprabasal and stratum corneum layers. The pigmentation is intensified by Wood's light examination. Dermal melasma reveals a preponderance of melanophages in the superficial and deep dermis which is not enhanced with Wood's light. Epidermal and dermal pigment alterations are present in the mixed variety. Indeterminate melasma is described in individuals with skin type VI in whom Wood's light examination is of no benefit.[8]

The prognostic significance of this classification is of key importance to the beneficial effect of treatment.Patients with epidermal type respond better to the use of depigmenting agents.However, in case of dermal melanin depositions, elimination of pigment is governed by transport via macrophages and is not accessible to depigmenting agents. Historically, the treatment of melasma has been challenging.Since it is a cosmetic problem, it can cause great emotional suffering. At present, there is no universally effective agent for the treatment of melasma. There are, however, various therapeutic modalities that can offer a significant benefit.Besides camouflaging the melasma patches, many agents have been used to eliminate the excessive pigmentation. However, before attempting to treat melasma , it is important to keep in mind the factors that are associated with the abnormality of pigmentation. First, there is an increased proliferation and therefore an increased number of melanocytes. Second, the melanocytes exhibit enlarged perikarya and increased arborization of their dendrites. Finally, there is an increased transfer of melanosomes to the basal and suprabasal layers.

Accordingly, the objects of the melasma therapy should be

a) retardation of the proliferation of melanocytes
b) inhibition of melanosome formation and
c) enhancement of melanosome degradation

GENERAL MEASURES

As solar exposure exacerbates melasma, its avoidance is fundamental to successful management. Broad spectrum sunscreens should be used.[9] Patients on oral contraceptives must discontinue their use.

BLEACHING AGENTS

a) Phenolic compounds(4-Isopropylcatechol and 4-hydroxyanisol)

They are metabolized by tyrosinase to radicals which are cytotoxic to the melanocyte. The combination of 4-hydroxyanisol(2%) and tretinoin(0.01%) results in effective skin lightening. Satisfactory results have been reported after the use of a phenolic thioether n-acetyl-4-S-cyssteaminylphenol in a 4% oil in water emulsion applied twice daily for 6 months.[10,11]

b) Vitamins C and E

Vitamin C promotes the conversion of melanin to colourless leucomelanin and has been used systemically in mild forms of melasma. Vitamin E seems to act

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synergistically to Vitamin C.[1]

c) Hydroquinone(HQ)

From the numerous agents that have been employed at different times for the treatment of melasma, hydroquinone seems to be one of the most effective.HQ concentrations 4% and 5 %are very effective but they are moderate to strong irritants. Results obtained with 3% HQ have been rated as "fair" to "good" in many patients and excellent in a few although a mild irritation maybe expected. 2% HQ concentrations are not irritating and their efficacy has been rated from "ineffective" to "very effective".[12]

d) Combination of hydroquinone and other agents.

It has been demonstrated that the skin lightening effect of hydroquinone can be enhanced by adding various topical agents such as tretinoin and corticosteroids. The following combinations have been proposed:

Formula I(Kligman and Willis)[13]

Hydroquinone	5%
Tretinoin	0.1%
Dexamethasone	0.1%

Excipient(solution containing equal parts of 95% ethanol and propylene glycol or a hydrophilic ointment).

Formula II(Pathak et al)[2]

Hydroquinone	2%
Tretinoin	0.05% - 0.1%

Excipient(equal parts of ethanol and propylene glycol)

Formula III(Katsambas and Antoniou)[1]

Hydroquinone	4%
Tretinoin	0.05%
Hydrocortisone acetate	1%

Excipient(equal parts of 95% ethanol and propylene glycol)

e) Azelaic acid

Azelaic acid, a naturally occurring straight chain saturated dicarboxylic acid, has been found to be beneficial in the treatment of melasma.[14]

CHEMICAL PEELING

Medium depth chemical peel results in a considerable lightening of the melasma patches and has been used alone for the treatment of melasma. However, chemical peel sometimes stimulates melanogenesis resulting in a worsening of the hyperpigmented patches.

LASERS

Laser therapy for melasma represents a novel approach to a vintage condition.However its efficacy and place in the treatment of melasma has yet to be established.

To conclude, the treating dermatologist must be constantly aware of the psychosocial impact of pigmentary imperfections, including those caused by melasma.Current therapeutic approaches are beneficial for many patients.However,they remain ineffective for some and cause significant side effects. Therefore, in the hierarchy of therapies for melasma, the treating dermatologist must establish a risk-benefit ratio for each therapeutic modality.

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UNTAMED HIV AND AIDS VACCINE.

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AIDS vaccine development has become an urgent need to control the global epidemic of HIV-1 infection, to combat this rapid spread of HIV, lots of research work has also been conducted for effective vaccine developments and their trials.

Despite the normal immune response few individuals show HIV positivity(123)'. Realistically this means that vaccine induced immune responses should clear all HIV 1 infected cells quickly before secondary spread occurs and persistent viral infection is established[4].

Therefore the development of vaccine against the AIDS must be driven by a complete understanding of viral pathogenesis and immunity followed by a HIV vaccine strategies[5] like.

a) What type of immunogen is needed for an effective HIV-vaccine
b) What do we have now and
c) What do we need to accomplish in future studies.

HIV STRATEGIES

The main three life strategies exhibited by HIV, a lenti RNA Retro virus which attack mostly T_4H-CD_4 cells are also a major obstacle in production or development of safe and potential HIV vaccine.

I) TROJAN HORSE STRATEGY [Latency]

II) DISGUISE STRATEGY [Variability]

III) CAMOUFLAG [Low immunogenicity]

TYPES OF VACCINES

1995, 1996 onwards proved to be the years of turning points in AIDS vaccine developments, which gave a ray of confidence in Scientist that a feasible AIDS vaccine can be prepared were.

a) Survival of HIV infected patients will increase for 5-10 years after post HIV infection.
b) Finding of a V3 – loop which is a relatively constant surface structure.

But as the very well known notion that "man proposes and good desposes" the same happened in the way of development of a feasible HIV- vaccine which make scientist to face the other obstacles (6) (Table I) and that motivated the researchers to take up this formidable challenge for development of HIV- vaccines which could be[6]

(Table II)

a) Killed whole virus
b) Live attenuated virus
c) Recombinant envelope sub component vaccine
d) MNrgp 120 with monoclonal or polyclonal antibodies, development of these vaccines and their trials were carried on
   I) Animals i.e Rhesus monkey, Chimpanzees, Macaq ues (pig tailed) and Gibbon apes or II) Human volunteers[7].

The Candidate vaccine to be produced are either

a) Prophylactic or pre exposure vaccine which can be used for general treatment as well as for babies borne to HIV positive pregnant mothers or
b) Immuno therapeutic or post exposure vaccine . But these vaccines have to be potential against AIDS to reduced severity of infection, complete prevention from infection and should be able to avoid integration of viral genome into host DNA (4,6). The sort of immunity aimed for vaccines which should have the principal goal to date has been a vaccine against HIV which elicits.
   I) Sterlizing immunity were vaccine would induce immune response that inactivate virus immediately after his entry, then its complete eradication before its establishment for persistent infection and action of neutralizing antibodies on the other hand the
   II) Disease limiting immunity were the vaccine would induce immune response that do not prevent infection but do reduce the viral load to low levels and thereby inhibit the development of disease and minimise infectivity by involving T-cell activation and production of neutralizing antibodies[7].

FAILURES

The failures of vaccines are resulted due to

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a) less protective efficacy of recombinant gp-120 vaccines.
b) Uncertainty to use viral strain and
c) Suspended clinical trials.

Table I : Obstracles in HIV vaccine development

1. Antigenic diversity and hypervariability
2. Mucosal route disease transmission
3. Infected cell virus transmission
4. Viral genome integration
5. Lentivirus
6. Sequestration in CNS
7. Ineffective host immunity
8. Dysfunction and destruction of host immunity
9. Animal studies correlation to human beings
10. Ethical, Social and legal issues
11. Limitations in using Human volunteers

Table II: Types of HIV vaccines

1. Candidate HIV vaccine
2. Whole inactivated vaccine
3. Live attenuated vaccine
4. Live recombinant vaccine
5. Virus like partial vaccine
6. Subunit vaccine
7. Synthetic vaccine
8. Anti idiotype Base vaccines
9. Nacked DNA vaccine

But the story of success and future of vaccines lies under clinical trial on HIV positive patients and development of a potent adjuvants and use of canary-pox as a alternative live replicating vector[4].

CONCLUSION

There is no doubt that an effective AIDS vaccine would be a major assets in global AIDS programme designed to stop the spread of HIV infection and that it warrants all our efforts unless we find a means to reverse the present trend.

The AIDS epidemic will irreparably damage many societies and could turn into an epidemiological catastrophe[5]. Since there are no "quick fix" alternative to the HIV vaccine problems and none should be expected so soon[6].

Hence it emphasised a fact that let us look at AIDS not as a Horror story but as an evolutionary process. A stage at which Homosapiens must learn to be a more responsible species.

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MYCOBACTERIOLOGY LABORATORY - ROLE AND RESPONSIBILITIES

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The microbes never fail to surprise like terrorists they go underground, formulate fresh strategies and strike again whenever the conditions are conducive. Mycobacterium tuberculosis has been no exception and taking advantage of our complacency has once again struck, the whole world, this time with an armamentarium of drug resistance. Unfortunately our laboratories, which are the only places that act as sentinels, were taken unawares and most of them did not even possess the expertise to detect the deadly new development.

It was not until two decades ago that the medical community, particularly in developing countries, reawoke to the fact that the role of mycobacteriology laboratory is not restricted merely to smear examination but is much wider. A mycobacteriology laboratory plays a major role in breaking the chain of events that lead to the transmission of disease in the community. It begins with education, isolation, identification and drug susceptibility report on the etiological agent and ends with epidemiology, surveillance and research. Timely report on the isolate helps not only in the management of the patient but also initiates the process of contact tracing, detection and prevention of outbreaks. During the past decade, the laboratory diagnosis of tuberculosis has undergone a revolution and the use of modern technology has ensured that the reports on acid fast bacilli examination reach the clinicians within 24 hrs, identification of tuberculosis within 10-14 days and drug susceptibility tests within 15-30 days of specimen collection[1]. Smear microscopy is the cheapest method of diagnosing pulmonary tuberculosis but its efficacy is limited only to sputa containing at least 5 x 10^3 tubercle bacilli/ml of material.

This is main - stay of our NTP and rationale is that for all practical purposes smear negative cases are not infectious[2]. It has been reported that almost 50% of the cases detected in any epidemiological survey are culture +ve and smear –ve. Moreover around 25% of these culture positive subjects are also radiologically negative(3). Culture has the added advantage of examining the isolate for drug susceptibility which acts as an important epidemiological tool. It is quite understandable that culture facilities are not feasible at the periphery but it is equally important that the medical officers are made sensitive enough to refer either the patient or his sample to the nearest laboratory which performs the test particularly if the patient is symptomatic with cough of more than 2 weeks duration or is not responding to chemotherapy. The bacilli in the sputum can remain viable at room temperature for 3 days with minimal loss of viability and 7 days with some loss of viability and culture can detect as few as 10 viable bacilli in the specimen.

Team work

No laboratory can work in isolation. Even the most sophisticated laboratory with fully dedicated workers will be helpless if the clinicians fail to provide good and adequate specimens. Diagnosis of TB in a patient is a team work where the laboratory and the treating physician must work hand in hand, which is generally not observed. It is a well established fact that three consecutive (2 spot and one home collection) sputum smear examination are almost equivalent in sensitivity to culture, but the laboratories rarely get more than one sample from the suspected symptomatic patient.

Laboratory responsibilities

An efficient laboratory recognises that delay in diagnosing TB not only prevents the patient from getting proper chemotherapy but also seriously hampers public health control measures. The patient continues to infect others and creates a pool in community which is dangerous particularly if the case is of multi-drug resistant TB. The laboratory must also realise that it has to remain well versed not only with technique but the total disease scenario as well. The picture of TB with AIDS is totally different from the conventional TB. Sputum examination may be negative in these patients while blood and stool may be more useful specimens.

Maintaining quality control is another major responsibility of the laboratory. While investigating, the laboratory must ensure that the positivity is not a result of contamination either at the source or in the laboratory. In

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the laboratory the bacteria are often transferred from a positive slide on to a negative slide either during the staining procedures or if the oil dropper is allowed to touch the slide or if the microscope objective has not been wiped properly after the examination of slide. In Indian Department of Biotechnology, Govt. of India has recently established mycobacterial repository centre at Central JALMA Institute, Agra which has epidemiological characterisation of strains by molecular method as one of its objective. All laboratories must ensure safe environment for their staff. Transmission of TB results essentially from inhalation of 5 um diameter size aerosols containing tubercle bacilli. It has been reported that the risk of disease is 2-5 times more in laboratory workers than the general population. Every individual in the laboratory should be so trained that his/her techniques do not give rise to aerosol formation. With these potentially dangerous droplet nuclei. he/she should feel responsible for his/her own safety and that of his/her co-workers. The pride of the laboratories should be in possessing biological safety cabinets with high efficiency particulate air filters rather than air conditioners.

Status of mycobacteriology laboratories

Based on the suggestions of WHO and IUATLD, Mitchison recommended 3 types of laboratory systems for the developing countries; peripheral, intermediate and central.

1. Peripheral laboratories perform only direct smear. Microscopy and are attached to PHC used to cater 1 lakh population and has in addition x-ray facilities also. Now they are replaced by CHC catering the population of 30-40 thousand.
2. Intermediate laboratories do smear microscopy and may inoculate culture media for transportation to a central laboratory. These laboratories may be in district hospitals.
3. The central laboratories are like reference laboratories fully equipped to do smear microscopy, culture, identification, drug sensitivity and research. They also take up the responsibility of organizing training and quality control programmes.

It is time we should conduct survey in our Kashmir to assess the status of our tuberculosis laboratories, since TB is re-emerging back. Although laboratories are there but without facilities. Smear microscopy being main diagnostic method, this also lacking perfection in our peripheral laboratories. The standard procedures like culture, sensitivity and identification of the mycobacteria are missing in our reference centre also.

It will be needless to repeat that tuberculosis today is the leading killer out of all infectious diseases and if we want to control it, strengthening of mycobacteriology laboratories is equally important which we have neglected. It is not necessary to provide all laboratories with modern equipments but it is important to assess their status and bring them all up to a certain acceptable standard for which training is a must.

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SAFE BLOOD AND ITS RATIONAL USE

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Introduction

Blood transusion by and large is a life saving procedure. A blood transfusion service is the lifeline of any hospital, without which efficient medical care can neither be assured nor can be sustained[1]. There is hardly any subdivision of medicine, which does not require use of blood or its components at one stage or the other. It is therefore of paramount importance to provide blood that delivers the required therapeutic component but whose transfusion entails little or no risk of an infectous or non-infectious adverse event[2]. The article concerns with basic concepts of blood safety and its rational use.

Transfusion Transmitted Diseases[3,4,5,6]

Blood transfusion is always associated with risk. It can never be made 100% safe (Transfusion transmitted infection, window period, cost, quality control). More than 400 microoganisms can use blood as a vehicle for transmission[7]. Table 1[8] gives the list of main diseases transmitted through blood.

Table-1

Viral	Bacterial	Parasitic
Hepatitis B virus (HBV)	Syphilis Brucella	Malaria
No-A, Non-B Hepatitis (NANB)		Toxoplasma
Hepatitis C Virus (HCV)		Microfilaria
Hepatitis G (HGV)		
Human Immunodeficiency Virus (HIV)		
Epstein Bar Virus (EBV)		
Cytomegalo Virus (CMV)		
Human T lymphotropic Virus (HTLV - 1 & HTLV- II)		

Viral Hepatitis

Viral hepatitis is one of the serious complications of blood transfusion and can be due to different infectious agents like hepatitis A, B, C, D, E and G virus (HAV, HBV, HCV, HDV, HEV, HGV) besides cytomegalovirus (CMV) and Epstein Bar Virus (EBV). Post transfusion hepatitis is mainly due to hepatitis B virus and hepatitis C virus which earlier used to be non A, non B hepatitis. There are about three hundred million hepatitis C carriers in the world. Unfortunately most of the carriers of hepatitis are not even aware of their carrier status.

Hepatitis A Virus

Transfusion of hepatits A virus by blood transfusion is rare because of two main reasons:-

i) Presence of virus in blood for short time.
ii) Carrier state is very rare.

Hepatitis A virus circulates in blood only during the initial acute phase of infection and during this period the individual is not the candidate for donation of blood. However viremia may be present before the development of symptoms and blood donated during this period could be infective.

Hepatitis B Virus infection (HBV)

It is important causative agent of transfusion-associated hepatitis. Humans are the only reservoir of hepatitis B virus. The virus is infective and minute amounts as little as 0.00001 ml can transmit the infection.

Presence of HBSAg in a patient wth post transfusion hepatitis, however does not necessarily indicate transfusion associated HBV infection since presence of HBSAg may be due to a preexisting carrier state rather than recent infection. The presence of Ig M anti-HBC which is positive in recent infection but not in chronic infection is the only serological test that reliably diagnoses transfusion associated infection.

Secreening Tests for HBV

Currently most sensitive and widely used tests for detection of HBSAg are based on EIA (enzyme immunoassay) /ELISA (enzyme linked immunosorbant assay) princple. In India unfortunately many blood banks especially those with little or no blood in the quarantine stage and having walking donor programme are compelled by the circumstances to use rapid screening tests for detection of HBSAg. As these test procedures are based on latex agglutination or chromatographic principles, whose sensitivity is low, a large no. of HBV blood units are cleared for transfusion and thus the infection gets

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transmitted to unluckly patients. Even iafter using the most sensitive screening tests for the detection of HBSAg in blood from voluntary donors, HBSAg -ve units have been found to transmit the hepatitis B virus infection. The basic aim of blood transfusion services should be to provide zero risk blood for transfusion, however in actual practice this is not achievable because of following reasons:

1) Lack of test which is 100% sensitive.,
2) Failure to detect HBSAg in some donors in the early incubation period.
3) Difficulty in carrying out highly sensitive test like DNA Hybridization and Polymerase chain reaction (PCR)

Extensive studies have shown that exclusion of blood units with isolated high titers of anti HBC (even HBSAg negative) are effective in markedly reducing the chances of post transfusion hepatitis B iinfection. This fact led some of the blood banks to incorporate the testing for anti-HBC in the donor screening protocols. This strategy is not adopted in our country and most of our blood banks restrict screening for hepatitis to HBSAg alone.

Hepatitis C

HCV is the most common cause of post transfusion non-A, non-B hepatitis in the developed world.

Screening Tests for HCV:

The detection of antibodies for HCV is used for the serodiagnosis of HCV infection. It is too early to comment whether hepatitis C (HCV) is the only cause of parental NANB hepatitis as the current HCV antibody assay fails to detect NANB hepatitis. Currently about 6% of blood banks test the donor blood for anti-HCV in India[9].

Hepatitis D

Although tests for Delta antigen and antibody are listed but should not be used in blood donor screening as all infections with delta virus are positive for HBSAg, so routine testing for HBSAg will eliminate risk of transmission.

Prevention of Post-Transfusion Hepatitis

It can be done by:

1. Promotion of voluntary blood donation.
2. Proper donor interview and selection.
3. Use of most sensitive and specific tests for HBSAg detection (3rd generation tests).
4. Screening for antibody to hepatitis core antigen (anti-HBC)
5. Screening for anti-HCV to detect carriers of HCV.
6. Good manufacturing practices (GMP) for blood fractionation and incorporation of virucidal technology (solvent detergent technique) for viral inactivation.

Human Immunodeficiency Virus (HIV)

The HIV-1 and HIV-2 are lentiviruses, etiologically responsible for AIDS. Though transmission of HIV through infected blood and blood products contributes to only 5-7% of total HIV infection in the country, the efficiency of transmission through this route is as high as 90%, that is if 100 persons are transfused with infected blood and blood products, 90% of them are expected to get the infection. It is important to note that this mode of transmission of HIV is entirely preventable. The testing of HIV in donor blood is currently being practiced in 95% of the blood banks. Detection. of antibodies to HIV-1 and HIV-2 is an accepted method for identification of HIV infected blood donations. For transfusion purposes single ELISA/Rapid/single test for HIV is mandatory and sufficient criteria in India.

Table-2: Prevalence of Various infections in Blood donors in India[10]

Infection	Voluntary donors (39%)	Replacement donors (58%)
HBV	1.6%	2.03%
HIV	0.77%	0.71%
Syphilis	0.49%	0.55%

Table-3: Prevalence of various infections in blood donors in Kashmir

Infection	No. Screened (Voluntary + replacement)	Frequency/1000
HBV	12919	3.8/1000
HIV	22196	1.26/1000
VDRL	0.00%	0.00%

Malaria

Examination of blood film is not suitable for screening large no. of blood donations because it is difficult to find parasites in blood film in short time especially if density of parasite in blood film is <100 per micro liter of blood. Testing malarial antibody by indirect fluorescent antibody (IFA) or ELISA is suitable screening for non-endemic areas but not ideal for malaria endemic areas e.g. India. Sensitive tets using monoclonal antibodies for detection of malarial antigens are available but are costly. Some experts suggest that malaria chemoprophylaxix should be give to all receipients of blood in highly endemic areas.

Cytomegloviruis (CMV) Infection

More than 50=80% of adults in developed countries and almost 100% in some underdeveloped countries have antibodies to CMV, so screening of all donors is not practically feasible. However blood transfusion services

should have panel of CMV negative blood donors. In high-risk patients e.g. patients of bone marrow transplantations or patients with HIV infection it is advisable to use anti-CMV negative blood or use leukocyte-depleted blood. The latex agglutination test is an appropriate screening test mostly used in many blood transfusion centers because of being rapid and simple. In India the testing of donor blood for CMV is not routinely practiced.

Syphilis

Blood transfusion is a potential route of infection, preferably if fresh infected blood is transfused. The incubation in transfusion syphilis is on the average 9-10 weeks and usually exhibits as secondary eruptions. Spirochetes are very sensitive to temperature and die at lower temperature e.g. storage of blood at 2-6°C for 72 hours prior to transfusion kills all spirochetes. However even if blood is refrigerated but has >$2.5x10^7$ spirochetes / ml, it will remain infective for five days.[10]

VDRL test is simple, rapid, non-specific and economical test for screening syphilitic infection. However the test needs inactivation of the specimen (sample) and the shelf life of reconstituted antigen is poor. RPR is a macroscopic non-treponemal flocculation test for screening syphilitic infections. The test is rapid and does not need inactivation of sample and the antigen used is a modified VDRL antigen (cardiolipin) In India 65% of blood banks routinely test the donor blood for syphilis (most of them use VDRL or RPR)[10]

Creutzfedt-Jakob Disease (CJD)

Although transmission of CJD through blood and blood products has been speculated but no case has been reported. Individuals at risk CJD i.e. persons who have received tissue or tissue derivatives known to be agent (e.g. pituitary growth hormone of human origin, durameter) or persons with family history of CJD are excluded from donating blood.

Human T-Cell lymphotrpic viruses (HTLV)

The virus is transmitted by transfusion of cellular components of blood but not by cell free components like plasma. The antibodies to HTLV become detectable by 14-30 days after transfusion but may take as long as 98 days. It is reported that the risk of HTLV decreases with age of cellular blood components. Several HTLV screening assays are available like gelatin particle agglutination (PA), enzyme immunoassay (EIA) and indirect immunoflorescence (IF). Universial screening of blood donors for HTLV was introduced in December 1988 in USA and in July 1991 in France.

Viral Inactivation Strategies[11]

Three most commonly employed methods are;

1. Pasteurizations (heating in the liquid state)
2. Dry heat (heating in the lyophilized state)
3. Solvent detergent method: it is best method of eliminating the infectivity of enveloped viruses but non-enveloped viruses is unaffected by this technique.

Newer Methods;

Short wave ultraviolet (UVC) with or without addition of antioxidants (e.g. flavinoids)[12,13]. Solvent detergent with UVC irradiation kills HBV, HCV, HIV and hepatitis A viruses.

Legal frame work and the court judgment in revamping blood banks

Schedule XIIB of the drug and cosmetic Act/rules stipulate mandotory testing of blood for blood transmissible diseases like malaria, syphilis, Hepatitis B, Hepatitis C and HIV. The rules have been recently amended providing for adequate testing procedures, quality control, standard qualification and experience of blood bank personnel, maintenance of complete and accurate records etc. The Drugs Controller General (India) is the central licence approving authority whereas the regulatory control remains under the dual authority of state and central government. The blood banks under this act require manufacturing license.

Supreme court of India in its historic judgment on 4th January 1996, directed Union of India and state governments to take various steps towards co-ordinated management and revamping of blood banking activities in all its facets of collection, testing, quality control, storage, archiving, rational use, monitoring, training and research. Follow-up of the judgment was the formation of National Blood Transfusion Council in May 1996.

State blood Transfusion council has been set-up in all the states and union territories. Only licenced blood banks are supposed to function in the country. Professional blood donation has been banned from Ist January 1998. Section 80-G of the income tax has been amended by the government to provide exemption for 100% deduction from total income to the donors in respect of donation to the national and State councils.

Rational use of Blood

The requirement of blood in our country, assessed on the basis of number of hospital beds with a criterion laid down by WHO of 6-16 units (average II units) of blood per hospital bed is estimated as 60.00 lakh units per annum. There is overall shortage of blood to the extent of 50% at the existing level. It is likely that shortfall will increase in future. Nearly 30-60% of unnecessary transfussion indicates a need for awareness of clinicians.

Blood component therapy is appropriate, effective as it gives the patient only what he needs and blood component harvesting from a single unit of blood can be used for

various purposes, thus optimising the use of same unit of blood.

Approaches to minimuze the use of blood and blood products in the management of blood loss

- ❑ Loss of blood is not an indication for the replacement of blood.
- ❑ Replace blood wherever blood loss is life threatening.
- ❑ Restore blood volume.
- ❑ Maintain adequate supply of oxygen
- ❑ Care of general condition (pain, injury, fever, urine output)
- ❑ Monitor temperature, pulse, blood pressure, and CVP.
- ❑ Blood/plasma substitute to be given in right amount.
- ❑ Monitor urine output 0.5 ml/kg body weight (adult aprox. 30 ml/hr)
- ❑ Use intraoperative blood salvage

Single Transfusion[3,4]

Availability of blood makes it easy for the surgeons and physicians to order single unit of blood without giving due thought to the indications and hazards associated with it. The request for single unit blood transfusion in surgery is common practice in India, which by and large has been seen as an act of thoughtlessness. It is important that we should avoid the use of single unit blood transfusion in surgery and conserve the essential commodity for use in other needy patients. Transfusion trigger may be lowered to 7.5 gms/dl Hb value and should be based on rate of development of anemia and assessment of its effects on prognosis.

Autologous Transfusion[3,4,10]

It is the collection and subsequent reinfussion of the patient's own blood or blood components. This technique is used alone or in combination to reduce or eliminate the need for homologous blood and is most effective in elective and planned surgery. There is no risk of transfusion-transmitted infections, no immunologic reactions and it affords greater flexibility in use.

Various options are:

Preoperative autologous donation, acute isovoluemic haemodilution, intraoperative blood salvage, postoperative blood salvage.

Role of General Practitioner for pregnant woman[6]

1. Reduce blood transfusion by increasing iron stores of pregnant woman so that blood loss during delivery is treated better.
2. Regular prophylactic iron and folic acid (IFA) tablet supplementation and consumption of foods rich in green and leafy vegetables.
3. Prescribing therapeutic IFA tablets or injectable iron to pregnant woman with severe anemia.
4. Diagnosing and treating as early as possible, anemia, and diseases which cause anemia such as malaria, hookworm, and other parasitic diseases.
5. Using antimalarial for chemoprophylaxis in areas where malaria is highly endemic.
6. During delivery ensure minimal blood loss by cutting short the third stage of labour and by use of oxytocin.
7. In case of acute blood loss in a pregnant woman during delivery, encourage immediate replacement of fluids by use of normal saline and plasma expanders especially if her Hb status prior to delivery was good. Only woman who have both low Hb and symptoms of acute blood loss or severe anemia (Hb=<7.5 gms%) with failure would require blood transfusion. In such emergencies timely intervention is critical for saving life. Immediate oxytocin followed by plasma expanders and rapid transportation to a place where facility of transfusion of tested blood is available will save a precious life.

Fresh Blood[2,3,4]

Fresh blood is defined as whole blood, reduced plasma, or concentrated red cells less than one day old. Use of freshly drawn blood less than 24 hours old is a VESTIGE of the old transfusion practice when appropriate components were not available. Processing donor blood that includes typing ABO and Rh antigen, antibody screening tests for HBSAg. HIV, HCV, Syphilis, Malaria is rarely complete in 24 hours. On storage of blood in CPDA-1 solution for 35 days, the red cells have about 80% post transfusion viability, which is accepted, standard all over the world. Presently there is no rationale for recommending fresh blood transfusion.

Promotion of voluntary blood donation

All blood donations should ncessarily be voluntary and non renumerated. There is need to educate all members of the community especially youths that blood donation is safe and does not cause any weakness or disease. Blood donated is rapidly replaced by the body and that a healthy individual can donate blood once in 3 months. Since we have to put a stop to the commerical blood donation system, steps will have to be taken to mobilize the mass media and to establish a one to one communication in a big way, at the same time ensuring infrastructure support and safety.

Some facts and myths about blood transfussion[6]

Facts:

1. There must always be sound reason for blood transfuion in any patient:
   a. Blood transfusion is indicated when blood loss exceeds 30% particularly in patients with massive

internal or external hemorrhage.

b. When the estimated blood loss is between 20-30% plasma expanders (crystalloids or colloids) can be substituted for blood
c. An adult can tolerate loss of blood up to 30% without blood transfusion.

2. In adults one unit of blood (450ml) will increase the Hb up to 1 gm%
3. The collected blood can be used within 28-35 days depending upon the anticoagulant used.
4. Every healthy individual in the age group of 18-60 years with Hb not less than 12.5 g/dl can donate blood once in 3 months.
5. Donor with history of jaundice in the past one year, STD's, Heart disease, major surgery in past six moths, malignant disease, active tuberculosis and epilepsy should not donate blood.
6. Women in pregnancy and lactation are deffered as blood donors.
7. Donors having history of malaria diagnosed on the basis of malarial parasites in the peripheral blood and who have been duly treated or have taken antimalarial drugs may be accepted after 3 months.
8. In order to ensure safety of transfused blood autologous blood transfusion is encouraged particuilarly for planned surgery.

Myths

Blood donation causes weakness or disease.

Conclusion

Availability of safe blood and blood products is a basic requirement of health care programme. Blood transfusion has undoubted benefits but it also carries serious risks of transmission of infectious agents e.g. hepatitis B, C, Syphilis, Malaria & AIDS. Efficiency of transmission of HIV through blood is more than 90%. It is important to advocate the policy of fewer transfusions, safe donors, and safe screened blood for transfusion. All blood donations should be voluntary and non-remunerated. All blood banks should have facilities/provisons for carrying out mandatory tests for blood transmissible infections e.g. hepatitis B, C, HIV, VDRL for Syphilis and Malaria. Autologous blood transfusion and use of blood components rather than whole blood should be encouraged. There is need for donor awareness programme and donor deferral practice, centralization and reorganization of blood banks services is necessary. Internal and external quality control for serological screening and auditing of transfusion services should be routine and mandatory.

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"BREAST FEEDING. THE NATURE'S WAY".

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Breast feeding has been the most natural response of a mother to satisfy the emotional and nutritional need of her infant. That this can serve as a natural barrier to infections and even save us money, is perhaps not thought of. It becomes important because health programmes have interpreted breast feeding as a preventive and promotive measure. The affectivity of the breast milk has long been established for reducing diarrhea, pneumonia, improved child nutrition and development along with its potentials in child spacing.

World Alliance on Breast feeding Action (WABA) is stressing on the theme that breast feeding is the most natural and correct way of nurturing a human infant. In addition to the various invaluable health benefits of breast milk, it is clear that breast feeding is a totally eco-friendly practice.

On the other hand bottle feeding which is still widely practiced is not only damaging to the life and health of millions of unfortunate infants, but also hostile to the environment and national economy Right from raising cattle to manufacture of formula, to consumption by target population and waste disposal, the practice of bottle feeding harms the ecology significantly.

According to National Health Survey the rate of exclusive breast feeding in India was only 50.9% upto the age of 3 months and only 26.4% in 4-6 months age group. The major reasons for decline in breast feeding practices in India are:-

1. Rapid urbanization and following the practices of elite class.
2. Commercial pressure by marketing companies giving wrong information.
3. Lack of self confidence in mothers.
4. Practical problems of working mothers.
5. Above all inadequate training of medical students and health personnel regarding practical aspects of lactation management. Experience from countries like Brazil, Maxico and Honduras, have shown that investing in promotion of breast feeding is among the most cost-effective health intervention for child survival equal to conventional practices like immunization, vitamin A supplementation and ORT.

"ECONOMICS OF BREAST FEEDING"

Breast milk is almost priceless. Investments made on promotion of breast feeding are bound to reduce the expenditures used in other health case sector and provide better returns.

The economics of breast-feeding is a new perspective, which may further enhance its perceived value among the policy planners. However, efforts have not been made to look into the potentials of investments to be made in this area, with wide scope of savings and returns not only in economic terms but in terms of building a healthy nation with wide ranging progress avenues being opened up. While the value of manufactured baby food is calculated in Gross National Product (GNP), the value of breast milk is not, which is significantly very high.

Assuming that an average Indian mother lactates for 2 years with daily milk out put of 600 ml, thereby the approximate amount of breast milk produced over these 2 years per mother would be 346 liters. The annual births in India are 24-33 millions. An infant mortality rate of 73 would still leave 22.6 million infants alive. Accordingly, annual theoretical breast milk production capacity would be 8093 million liters. Due to improper feeding practices the annual realistic production is estimated to be nearly 4000 million liters valued at the cost of fresh animal milk (Rs.15/litre), the market value of this breast milk. Would be Rs. 6000 Crores and at the cost of tinned milk (Rs.30/litre), it would be Rs 12000 Crores. This amount in the context of central plan allocation, central budget 1998-99 of Govt. of India, the estimated value of breast milk at the cost of tinned milk is equal to allocation for each of Department of Industry, power and railways. It is three times the allocation for Education, Health and Family welfare and Science and Technology each.

"FINANCIAL BURDEN FOR FAMILY"

The cost of artificial feeding for the first 6 months, using powder milk would be around Rs. 6600 (Table I) this expenditure of Rs. 1100/month would definitely lead to a financial burden for family, equal to almost 43% minimum wages of a skilled urban worker, 25% salary of Class IV employee or 14% salary of trained graduate teacher. This

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is significantly enough to pinch the house hold budget of every family. On the other hand a lactating mother requires additional calories in form of 185 gms of Rice or 30 gms of pulses (Rs. 4/ per day) to produce one litre of milk. Also the high cost of artificial feeding would also render the baby to undergo malnutrition by over diluting the milk to save money.

"BREASTMILK IS GREEN AND BOTTLE FEEDING IS ECO-HOSTILE"

Breast milk and ecology are complimentary to each other. It is economical and requires no special packaging like formula milks and thus produces no pollution. Bottle-feeding is responsible for one and half million infant deaths and illness worldwide every year. The association of bottle-feeding with serious illness in babies was written as early as 1800s and it is now an established fact that bottle feeding in harmful to economy ecology and health.

An ICMR study in 1993 showed high intakes of heavy metals like lead, arsenic and cadmium and organochlozine pesticides by infants on formula milk feeds. Bovine milk contains high levels of DDT and HCH isomers because of spraying around cattlesheds and due to contaminated fodder significant amount of these chemicals are in dairy products, livestock meat etc. In addition, analysis of some infant formulas in U.K has revealed the presence of plasticisers called phthalates. These are endocrine disrupter chemicals and are linked with infertility both in males and females. Packaging also causes contamination with dioxins which are chlorine containing compounds that can damage immune system, initiate cancers, cause organ damage and birth defects. Polycarbonates in hard plastic bottle and affect the bottle-fed baby.

Breast-feeding produces no wastes, and problems of pollution are reduced. Kitchenwares and utensils are the source of lead contamination than breast milk.

"BREASTMILK AS ANTI-INFECTIVE AGENT"

Breastmilk provides many positive benefits for maternal and child health in both developed and underdeveloped countries. In underdeveloped countries, infants who are not breast-fed are 14 times more likely to die from respiratory infections compared to babies who are exclusively breast fed. Babies on bottle feeding experience more episodes of diarrhea and ear infections compared to breast fed infants.

Breast milk being free of contamination and adulteration, available at desired temperature has proven to be best anti-infective agent. The history of artificial feeding is one of the repeated failures. About a century ago, in an attempt to feed 130 babies in an orphanage in France, only 13 babies remained alive after 1½-year period, inspite of great care given to them. Even these 13 babies were severely malnourished. Anti-infective properties of breastmilk are attributed to certain immunoglobulins, Lymphoid cells, macrophages, lysozymes and compliments present in breastmilk particularly during first couple of days (through colostrum). Unsaturated lactoferin present in Breastmilk prevents enterobacteria growth. Low pH, high bifidus factors protect from E. Coli growth. Para-amino-benzoic ac id (PABA) provides protection against malaria.

"BREASTMILK WITH METABOLIC PROPERTIES"

Protein content of Breastmilk (1.1 gm/dl) is lower than in cows milk (3.3 gm/dl). Accordingly kidneys get low solute load, which suits their concentration capacity (lower during neonatal period). Breastmilk protein contains more lactalbumin, which is better absorbed than casienogen present in cow's milk. Breastmilk protein is less allergic than cow milk protein. Since the former is in micromolecular form and the later in macromolecular from and these macromolecules behave as allergens. Specific fatty acid pattern in breast milk promotes rapid brain growth.

Breastmilk benefits mother too, by reducing postpartum bleeding and helping involution of the uterus by being a natural method of birth spacing, by reducing the risk of ovarian and breast cancer and by increasing her self esteem as a nourisher and provider. It also helps in emotional bonding and generates the feeling of importance.

So keeping in view, economic returns, and other benefits of breast feeding, our aim should be to promote and support breast feeding as one of the best investment by raising public awareness on the economic value of breast feeding and high cost of bottle feeding and to provide concrete data on the economic, ecological and other advantages of breast feeding for public advocacy by organizing community groups discussions. Investing in its promotion is among the most cost-effective interventions for child survival, equal to conventional practices such as immunization and vitamin A supplementation and surpassing ORT(Oral Rehydration Therapy).

TABLE I :- COST OF BOTTLE FEEDING FOR A CHILD

	IM	2M	3M	4M	5M	6M	TOTAL
Bottle	76	—	—	—	—	—	76
Nipple	26	26	26	26	26	26	156
Fuel	20	20	20	20	20	20	120
Powder Milk	660	840	1020	1200	1200	1200	6120
Total (Rupees)	782	924	1104	1284	1284	1284	6472

M=Months.

The Baby Friendly Hospital Initiative (BFHI) has been successful in changing the hospital environment to promote

breast feeding through changes in delivery room protocols to promote early initiation of breast feeding, rooming-in, a ban on free gifts of infant formula or related products. Continued implementation and monitoring of the international code of Marketing of breast milk substitutes is needed to ensure protection of breast feeding, Government of India has enacted a law in this regard in 1992.

RECOMMENDATION AND ACTION PLAN

1. Spread awareness about benefits of breast-feeding through mass media; the print and audio-visual media can be used to propagate the message. Women's organization, Schools, NGOS, political parties and above all medical personnel and medical students should be given informative talks on the eco-friendliness of breast feeding and eco-hostility of bottle feeding and some can be passed on to masses through them.
2. Encourage formation of mother support groups, where expectant and nursing mothers need support and encouragement to continue breast feeding as long as possible. Explain health hazards, ecological harm and economical harm due to bottle feeding.
3. Doctors, environmentalists, toxicologists, agriculturists and media persons should work as team.
4. Pesticides should be used in a judicious way.

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MANAGED CARE

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Health care systems, though different, can be grouped into four 'archetypes'. Socialized medicine (as in Britain or Sweden) covers everybody, has a single payer, and usually has those who provide care salaried or capitated (paid so much for every person for whom they provide care). Socialized insurance (as in Australia, Canada, or France) also covers everybody and has a single payer, but puts those who provide care a fee for each service. Mandatory insurance (as in Germany, Malaysia, Japan, Singpore, Brazil) again covers everybody, but has multiple sickness funds or insuriance carriers and provides care through a mixture or salaried public providers and private providers paid a fee for each service. Voluntary insurance (as in the United States or South Africa) does not offer cover to everybody, and has many payers and providers and different systems of payment and delivery.

No heath care system in the world is stable. The drivers of change in the developed world are reaching the limits of the welfare state, exhausting traditional methods and tools for containing cost, and expecting increased consumer sophistication and demands. Change is being driven in the developing countries by the growth of the middle class, greater demands from that middle class, and the globalization of economics.

Changes in the United States are being driven by rising costs, failure to provide universal coverage, consumer dissatisfaction, and the increasing recognition that the country has poor life expectancy and high infant mortality despite expenditure on health care far higher than any other country. The main response in the USA has been the growth of managed care —the arrangement whereby an organization assumes responsibility for all necessary health care for an individual in exchange for a fixed payment; it involves a collection of techniques for containing costs and raising the quality of services.

Managed Care has been developed in response to every-increasing health care costs and dysfunctional fragmented services and covers a range of activities carried out in different organizational settings. It is continually evolving and works through changing clinical practice. Its continually changing nature and its diversity mean that managed care remains a slippery concept. Managed care is defined as a variety of methods of financing and organizing the delivery of comprehensive health care in which an attempt is made to control costs by controlling the provision of services.

Managed care developed in the United States as a response to a health care system lacking in coherence, suffering from organizational fragmentation, and consuming huge amounts of resources. Health care provision also suffered from a lack of preventive services, undertreatment and overtreatment of patients, and weak clinical accountability. The uncontrollable growth of medical care costs, and increasing evidence that prepaid group practices could provide comparable care at 20-40 per cent less cost, motivated government and large employers who financed insurance for their workers to look favourably on prepaid forms of health practice. Organized medicine saw the emergence of corporate medicine, and intermediaries between doctor and patient, as a threat to its potential profits and medical autonomy.

New insurance products have combined the idea of prepayment with greater flexibility and wider choice, and managed care is now growing rapidly.

Structure of Managed Care

The United States has so many different types of managed care structures that the system has been described as an 'unintelligible alphabet soup of three letter health plans.' Despite this, most managed care is carried out in one of the two basic types of organizational settings—health maintenance organization (HMO) or preferred provider organization (PPO).

A HMO (see box below) is a prepaid organized delivery system (a fixed amount of money is available to cover the health needs of members). The organization, therefore, assumes financial risk and may transfer some of that risk of doctors to other providers. Individuals enroll with a HMO and receive health care for a fixed premium.

The fastest growing form of HMO has been the independent practice association or network model, which now accounts for 70 percent of enrollment—about 35 million Americans. It offers patients a wider selection of doctors and other providers.

A PPO acts as an intermediary between the purchasers of health care and selected preferred providers, who agree to provide services on a discounted fee basis. Patients do not have to use the preferred providers in the plan but are

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encouraged to do so by a system of incentives and disincentives. PPOs technically are not managed care organizations; rather, they establish a network of doctors who serve an insured population on a reduced fee basis. They use a variety of strategies to monitor and control the provision of services.

As the insurance market place in the United States has become more competitive, these generic organizational types are being combined in many ways, making it difficult to differentiate one managed care oganization from another. Large managed care companies in competitive markets increasingly offer the entire range of alternatives.

The Process of Managed Care

There are three dimensions of managed care: health policy; systems management (how the policy is administered); and disease management (how diseases presenting to the system are dealt with).

Out of a global budget determined by makers of health policy and held by a managed care organization (an attempt at macromanagement of costs), providers are micromanaged within the system to ensure that they contain costs. More recently, providers have been micromanaged to ensure that quality is improved. Quality and cost control are becoming closely linked, and consequently the priorities of the managed care organization may become blurred. In addition, implicity in micro quality control is the promise of improving quality at a community level, that is, macro quality control. This is essentially the European perspective on managed care, which distinguishes it from practice in the United States.

The dimensions of managed care interact in the attempt to deliver quality health care while containing costs, but when all of the rhetoric is stripped away the common denominator is doctors. Managed care works only through modifying the actions of doctors (or other professionals initiating care) to eliminate inappropriate treatments and ensure that a cost effective-practice is adopted. A key aspects of HMOs is the use of primary care doctors to act as gatekeepers to specialized services. Clinicians' practice can be modified in three ways: developing networks and selecting preferred providers; supplying incentives; and providing guidelines; or by a combination of these.

Ways of Modifying Clinicians' Practice

Perhaps the best way of modifying the actions of doctors (or other professionals, hospitals, or alternative care settings) who waste resources or provide poor care is to ensure that they have no access to patients. This can be done by selecting specific doctors to provide services and providing incentives for patients to consult only these providers. The rationale is that only the 'best doctors' are chosen, who will then deliver the 'best care', ensuring that quality and cost be controlled. Doctors not performing to standard (however defined) are deselected. Many observers are concerned that profit oriented managed care companies will give priority to cost reduction and not quality of care.

The basic logic of managed care for a population is to put the financial risk onto health care insurance organizations and providers, and to give providers incentives to be judicious in the use of expensive resources. In some cases the health care insurance organization assumes responsibility for most of the risk but manages providers of health care through financial incentives, profiling patterns of service use, and other such strategies. Alternatively, the purchaser may transfer much of the risk to contracted groups by full or partial captation. Reimbursement may be combined with withholds and bonuses tied to doctors' performance. Some portion of remuneration may also be based on patient satisfaction, quality measures, outcomes (such a length of stay), turnover of patients enrolled, numbers of patients from the plan, and productivity. The potential for financial incentives to change clinical practice is well documented.

Clinical guidelines are a powerful way of modifying clinicians' practice and controlling the use of services. Managed care organizations use various utilization management strategies to control use of services. The basic idea is to review and supervise expensive decisions, ensuring that they accord with prescribed guidelines. Although guidelines are usually written by doctors, they are administered by case managers or coordinators, who are often nurses or managers. The most important types of utilization management are precertification of in-patient admissions review of length of in-patent stay or other expensive courses of treatment, management of high-cost cases, and second opinion programmes. Before admitting non-emergency patients to hospital or undertaking other specified expensive treatments, doctors should consult utilization management company and have the decision approved. After admission, a utilization manager monitors the in-patient stay or ensures the earliest possible discharge. In complex or difficult cases a case manager may work with the doctor to develop a treatment plan that substitutes less expensive care whenever possible. Utilization

management seeks to reduce health care costs primarily by avoiding unnecessary hospital admissions and reducing length of stay.

Most managed care plans use a combination of these methods. Doctor profiling and feedback on utilization performance, the use of formal written practice guidelines, and various types of utilization review are the most common.

Managed care in Europe

The European definition of managed care—'a process to maximize health gain of a community within limited resources by ensuring that appropriate range and level of services are provided and by monitoring on a case by case basis to ensure continuous improvement to meet national targets for health and individual health needs'— differs from most American definitions in that it promotes a community perspective and is seen as a joint task of policy makers, purchasers, providers, and receivers of care. The European view emphasizes community health gain as the starting point for the management of health care delivery; for the integration of the three levels of national health policy, community based management, and individual patent care management; and for disease management across all sectors of health provision.

Techniques of managed care in Europe

At the level of health policy, initiatives to improve the knowledge base of purchasing have been implemented in several European countries. These initiatives have created three dimensions for purchasing health gain: assessment of populations' health status and needs, evaluation of effectiveness of treatment and cost-effectiveness of services, and setting priorities. European health care systems vary in the way set priorities. In the tax based system of Scandinavia, priority setting discussions at country and regional levels seek to involve the public. In systems based on social insurance, such as in The Netherlands and Germany, discussions on health priorities have focused on the coverage of basic health insurance.

At the systems management level, provision of secondary health care is increasingly being based on the contracting mechanism between commissioners and providers, resulting in performance oriented payment using case mix groupings and quality specifications. Primary care physicians are recognised as gatekeepers to, or even commissioners of, secondary and community care as the starting point for effective purchasing.

At the disease management level, effective strategies are increasingly based on guidelines for medical treatment. Managed provision of health care in the 1990s depended heavily on informations systems that support the application of guidelines and integrate them with measures of outcome research and quality assurance programmes.

Evolution of Managed Care

First Generation

- Retrospective utilization review
- Contracts with preferred providers
- Second opinion programmes
- Little consumer information or education.

Second Generation

- Proactive utilization review.
- Increased use of capitation and gatekeepers
- Prospective payment of hospitals.

Third Generation

- Sophisticated utilization management
- Management of high-cost cases
- Provider profiling
- Clinical practice guidelines
- Complex financial incentives
- Full capitation or risk.

Four Generation

(Features now developing in the United States)

- Increasing interest in health outcomes
- Health plan report cards (league tables)
- Improved information system and system monitoring.

Fifth Generation

(The end point toward which managed care is working)

- Anticipatory case management
- Community based needs assessment.
- Targeted disease management.
- Integration of clinical services
- Outcomes based reimbursement
- Informed consumers.

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1th March, 2002

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Subject: Regarding Indexing of your Journal for "IndMED": a Bibliographic Database of Indian Biomedical Research" http://indmed.nic.in.

Sir,

Please refer to your letter dated 30/01/2002 on the above subject. I am pleased to inform you that our "IndMED Journals Selection Committee (IJSC)" has finally selected "JK Practitioner" for indexing in IndMED. IJSC annually reviews journals for indexing in IndMED.

The indexing work would start from April 2002. I would request to send us copies of the journals starting from 1994 to 1999 and From Oct. 2001 till date. In order to expedite the processing of future issues, a single copy of the journal should be sent as soon as possible.

Any change regarding corresponding address may be communicated to us immediately.

With regards

Yours sincerely

Dr. GM Malik,
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ENDOTHELIUM IN VASCULAR DISEASE: PRACTICAL RELEVANCE TODAY

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Introduction

The endothelium represents an organ approximately 1.5 kg in weight and 700 m^2 in area, which is distributed throughout the body is involved in the control of the vascular tone and homeostasis. More than just a simple diffusion barrier between the intravscular space and the extravascular matrix the endothelium is a highly active endocrine, autocrine and paracrine organ, which synthesizes, releases, activates and/or inactivates various vasoactive hormones.

Abnormal endothelial function manifests in a variety of pathological conditions including atherosclerosis, hypercholesterolemia, diabetes, hypertension, cigarette smoking, and hyperhomocysteinemia. Endothelial dysfurction and impaired vascular reactivity represent an early, critical stage in the pathogenesis of atherosclerotic vascular disease. Recent insights into the pathogenesis of vascular disease and endothelial dysfunction have opened a new frontier that has implications for future therapies.

Vascular Endothelium

The vascular endothelium is a multifunctional organ system composed of metabolically active cells that regulate the blood flow in the vessels. The arteries consist of three layers: the innermost intima, the media and the outermost adventitia. The vascular intima is composed of a single layer of squamous cells (10-50 mm in diameter) that constitute the endothelium. These endothelial cells are held together by junctional complexes that regulate permeability and control cell-to-cell communication. The endothelium also serves a dual function in the control of vascular tone. It secretes relaxing factors such as, nitrous oxide (NO) and adenosine, and constricting factors like the endothelins.

Endothelium Derived Relaxing Factors/Nitrous Oxide

The first major insight into the importance of the endothelium as a modulator of vascular tone was the discovery of the response of rabbit aortic rings to acetylcholine and norepinephrine. Furchgott and Zawadzki[1] demonstrated that, when vascular endothelium was present, the rabbit aortic rings relaxed in response to acetylcholine. However, in the absence of endothelium this vasodilator response was abolished. This suggested the existence of a vasoactive substance, which was named endothelium derived relaxing factor (EDRF). The predominant form of EDRF is NO or a closely related nitrosylated compound.[2] Many factors have been shown to regulate the release of EDRF/NO from the endothelial cells: acetylcholine, norepinephrine, bradykinin, thrombin, vasopresin, histamine, serotonin, and shear stress. In addition to its vasoactive properties, EDRF/NO is a potent inhibitor of platelet adhesion and aggregation.[3]

Endothelins

The endothelins are a family of closely related peptides that consist of three distinct proteins; endothelin-1, endothelin-2 and endothelin-3. Endothelin is the most potent known vasoconstrictor. The vascular tone depends on a balance between the endothelins and EDRF/NO.

Endothelial Dysfunction

Endothelial dysfunction is one of the most important concepts that have developed over the last decade. Increasing evidence suggests that vascular endothelial injury is the critical step in the pathogenesis of atherosclerosis. Atherosclerosis is a complex pathological condition that is characterized by accumulation of modified low-density lipoprotein (LDL), local inflammation, and immune responses. These cellular changes lead to endothelial dysfunction and, ultimately, to the development of clinical events like angina and acute coronary syndromes.

Conventional risk factors for coronary artery disease (e.g., hypercholesterolemia, hypertension, diabetes, smoking and advanced age) have all been shown to be associated with endothelial dysfunction.[4-7] The total number of risk factors that an individual has also determines the degree of reduction in endothelium dependent vasodilator function.[8]

Aging is an independent risk factor for endothelial dysfunction. A decline in flow-mediated endothelial function has been noted in men older than 40 years and women older than 55 years.[9]

Considerable clinical and experimental data is currently available to support the hypothesis that elevated total and LDL cholesterol levels are associated with impaired endothelial function, independent of the presence of overt coronary artery disease (CAD).[10-15] Oxidative modification

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Table 1. Trials of cholesterol lowering therapy and evaluation of endothelial function

Study	*Baseline Cholesterol (mg/dl)*	*Circulation Studied*	*Intervention*	*Duration of intervention (months)*	*Effect on Endothelial Function*
Egashira [37]	272	Coronary	Pravastatin	6	Improved
Anderson [38]	209	Coronary	Multiple drugs	12	Borderline improved
Treasure [39]	226	Coronary	Lovastatin	6	Improved
Seiler [40]	300	Coronary	Benzafibrate	7	Improved
Yeung [41]	230	Coronary	Simvastatin	6	No improvement
Drury [42]	209	Brachial	Pravastatin	54	Improved
Tamai [43]	195	Forearm	Apheresis	1 hour	Improved
O'Driscoll [44]	254	Forearm	Simvastatin	1	Improved
Andrews [45]	202	Brachial	Multiple drugs	30	No improvement
Leung [46]	239	Coronary	Cholestyramine	6	Improved
Stroes [47]	354	Forearm	Multiple drugs	3	Improved
Vogel [48]	200	Brachial	Simvastatin	0.5-3	Improved
Goode [49]	373	Arterial ring	Multiple drugs	10	Improved
Vogel [50]	198	Brachial	Pravastatin	0.5-3	Improved
John [51]	278	Forearm	Fluvastatin	6	Improved
Fuentes [52]	251	Brachial	Mediterranean Diet/ NCEP-I Diet	3	Improved

of LDL significantly enhances this association. High levels of HDL cholesterol reduce the inhibitory effect of LDL on endothelium mediated vasodilatation.[16] The central defect in hypercholesterolemia appears to be the reduced availability of NO as evidenced by the fact that L-arginine restores endothelial function in hypercholesterolemic individuals, suggesting either impaired NO synthase or reduced availability of L-arginine.[17] Hypercholesterolemia has also been associated with increased endothelin production, which may play an important role in plaque instability.[18]

Hypertension is characterized by dysfunction of both the endothelium and vascular smooth muscle. In chronic hypertension, one finds impaired endothelium-dependent relaxation of the vascular smooth muscle cells[19,20] and increased endothelium-dependent constrictor activity.

The main cause of death in patients with diabetes is atherosclerosis. Endothelial dysfunction, which ultimately progresses to atherosclerosis, has been documented in those who have insulin resistance and diabetes.[4]

Infection and resulting inflammation can also cause endothelial dysfunction. In an animal model, infection with Chlamydia pneumoniae resulted in endothelial dysfunction.[21] In patients with coronary artery disease (CAD), an elevated level of C-reactive protein, a marker of inflammation, is an independent predictor of endothelial dysfunction.[22]

Obesity has also been shown to be an independently associated with coronary endothelial dysfunction. [23]

The association between these risk factors and endothelial dysfunction is strengthened by the observation that risk factor modification (i.e., cholesterol lowering, smoking cessation, exercise, homocysteine lowering and ACE-inhibition) improves endothelial function.

Endothelial Dysfunction and Vascular Disease

Endothelial dysfunction seems to be the earliest marker of atherosclerotic vascular disease. Several researchers have suggested that the loss of endothelium-dependent vasodilatory response may be a marker of atherosclerosis in the absence of angiographically demonstrable atherosclerotic lesions. Egashira et. al.[24] demonstrated that endothelium-dependent vasodilatation is impaired in patients with anginal chest pain and angiographically normal coronary arteries. Hasadi et. al [25] showed that endothelial dysfunction could also result in myocardial perfusion defects on Sestamibi scanning in patients with angiographically insignificant CAD, thus indicating that endothelial dysfunction can result in myocardial ischemia even in the absence of obstructive CAD.

Clinical Measurement of Endothelial Function

In vitro endothelial function is most commonly measured as vascular ring tension in response to varying amounts of acetylcholine. Three clinical techniques are commonly used to test endothelial function:

1. Measurement of changes in coronary artery diameter on quantitative angiography in response to acetylcholine infusion.
2. Measurement of changes in coronary artery blood flow by intracoronary doppler ultrasound (flow-wire) in response to acetylcholine.
3. Ultrasound measurement of changes in brachial artery diameter in response to flow-mediated induction of hyperemia.

The normal response of coronary arteries to acetylcholine infusion is vasodilatation and increased blood flow, a response that is reversed to vasoconstriction and

decreased blood flow when there is endothelial dysfunction. Flow-mediated vasodilatation has also been used as a non-invasive measure of endothelial function. Normally, one minute after the release of a 5-minute arterial occlusion by a blood pressure cuff, the brachial artery diameter increases more than 5-15%. An abnormal response consists of lesser degree of vasodilatation or even vasoconstriction in response to hyperemia.

Elevated blood levels of endothelins, adhesion molecules, and von-Willebrand factor have also been used as markers of endothelial dysfunction.[26]

Prognostic Impact of Endothelial Dysfunction

Endothelial dysfunction not only serves as an early marker of atherosclerosis but also carries clinical implications. Suwaidi et. al [27] found that in 157 patients with mild non-obstructive CAD, the incidence of cardiac events including death, myocardial infarction (MI), or need for urgent revascularization was significantly higher in patients who had severe endothelial dysfunction compared with patients who had mild or no endothelial dysfunction (14 vs 0% p<0.05). Similarly Schachinger et. al [28] in 147 patients after a median follow-up of 7.7 years, found that impaired endothelial function was associated with significantly higher incidence of death, unstable angina, MI or need for urgent revascularization. In their study of forearm endothelial dysfunction in 225 untreated, uncomplicated hypertensive patients (mean follow-up of 31.5 months), Ceravolo et. al [29] reported 29 cardiovascular morbid events. The rate of total cardiovascular events per 100 patient-years was 8.17 in patients with the least increase in forearm blood flow in response to acetylcholine infusion versus 2.02 in patients with the highest increase in forearm blood flow.

These longitudinal studies clearly indicate the need to identify endothelial dysfunction in patients who have risk factors for atherosclerotic vascular disease. Early appropriate interventions to modify these risk factors and to reverse endothelial dysfunction should be attempted in such patients.

Interventions to Improve Endothelial Dysfunction

A number of interventions have been shown to be successful in reversing or improving endothelial dysfunction: L-arginine therapy, correction of hyperlipidemia, estrogen therapy, antioxidants, reduction in homocysteine levels, and ACE-inhibitor therapy.

L-arginine Therapy

L-arginine, a physiological precursor of NO, can improve endothelium-dependent vasodilatation in patients with atherosclerosis and hypercholesterolemia.[30-33] In addition, long-term l-arginine therapy increases apoptosis of cells in the intimal lesions leading to regression of atherosclerosis.[34] Lerman and colleagues [35] designed a double-blind, randomized study to test the hypothesis that long-term, 6-month supplementation of L-arginine reverses coronary endothelial dysfunction in humans with nonobstructive coronary artery disease. Twenty-six patients without significant CAD on coronary angiography and intravascular ultrasound were blindly randomized to either oral L-arginine (3 g TID) or placebo. Endothelium-dependent coronary blood flow reserve to acetylcholine was assessed at baseline and after 6 months of therapy. After 6 months. in the subjects who were taking L-arginine, coronary blood flow increased in response to acetylcholine compared with the placebo group (149±20% versus 6±9%, P<0.05). This was associated with a decrease in plasma endothelin concentrations and an improvement in patients' symptoms scores in the L-arginine treatment group compared with the placebo group.

However, Blum et al. reported no improvement in either No bioavailability or in flow-mediated dilatation of brachial artery in 30 patients with CAD who were treated with L-arginine for one month.[36]

Lipid Lowering Therapy

Studies have shown that endothelial dysfunction can be attenuated or abolished with the use of a HMG Co-A reductase inhibitor, which might contribute to the reduced incidence of ischemic events seen with lipid lowering. Sixteen clinical trials have reported the effect of cholesterol lowering on endothelial function using a variety of therapies.[37-52] (Table 1) In 13 of these, endothelial function improved significantly with lipid lowering. Endothelial function improved within one hour of cholesterol lowering by LDL apheresis and within 2 weeks of starting therapy with a statin. Improvement was seen even in patients who had borderline elevated cholesterol levels. Improving endothelial function by lowering cholesterol may be an important component of plaque stabilization, which in turn may be responsible for reduced adverse vascular events seen after such therapy.

Antioxidants

Although oxidative stress appears to be important in the development and expression of endothelial dysfunction, the value of antioxidants in the prevention and treatment of atherosclerosis remains controversial. Data from the Alpha-tocopherol Beta-carotene study [53], HOPE trial, [54] and the GISSI study group [55] suggests a lack of benefit of vitamin E on cardiovascular events.

Inhibition of Renin-Angiotensin System

A number of studies have evaluated the role of ACE-inhibition on endothelial dysfunction.[56-60] The Trial on Reversing Endothelial Dysfunction (TREND) used a double-blind, randomized, placebo-controlled design to [illegible]

the effect of Quinapril (40 mg daily) on acetylcholine-mediated changes in coronary artery diameter using quantitative coronary angiography. The constrictive responses to acetylcholine were comparable in the placebo (n=54) and Quinapril (n=51) groups at baseline. After 6 months, only the Quinapril group showed significant net improvement in response to incremental concentrations of acetylcholine (4.5±3.0% versus -0.1±2.8% at 10^{-6} mol/L and 12.1±3.0% versus -0.8±2.9% at 10^{-4} mol/L, quinapril versus placebo, respectively; overall P=.002).

Erdothelial function improves primarily with use of agents that have a high tissue specificity for ACE, such as Quinapril.

Estrogens

Improvement in endothelium-dependent vasodilatation has been demonstrated in post-menopausal women after the administration of estrogens. [61-63] The predominant mechanism appears to be an upregulation of the synthesis of NO synthase. Another potential mechanism is reduction in coronary endothelin-1 levels. [64]

Homocysteine-Lowering Therapy

Thambyrajah et al. [65] recently reported on the results of homocysteine-lowering therapy with folic acid on endothelial function. In a randomized double-blind trial, 86 patients with CAD were treated with folic acid (5 mg) or placebo for 3 months. Endothelial function was assessed by measuring: 1) flow-mediated endothelium-dependent dilation (EDD) of the brachial artery; 2) combined serum nitrite/nitrate (NO_x) concentrations and; 3) plasma von Willebrand factor (vWF) concentration. At the end of the study, plasma homocysteine was lower in the folic acid group compared with the placebo group (mean 9.3 vs. 12.3 mmol/l, $p < 0.001$). Although there were no significant differences in EDD, serum NO_x or plasma vWF between the two groups, there was a greater increase in EDD from baseline in the folic acid group (1.2 vs. 0.4 % in the placebo group, P = 0.07). The absence of an unequivocally positive result may have been due to inadequate sample size or chance, underscoring the need for large randomized controlled trials before the implementation of routine folic acid supplementation.

Gene Therapy

A novel approach to improve NO bioavailability, adenovirus-mediated endovascular gene transfer of NO synthase isoforms, raises levels of NO synthase activity.[66] However the applicability of such treatment in human subjects at present remains uncertain.

Conclusion

Endothelial dysfunction, an apparent early marker of vascular injury, has been associated with all conventional risk factors of CAD and is found even in the absence of angiographically demonstrable atherosclerotic CAD. Endothelial dysfunction can be easily measured non-invasively by measuring flow-mediated brachial artery dilatation.

Of several therapeutic modalities currently available which effectively reverse or attenuate endothelial dysfunction, statins and ACE-inhibitor therapy seem to be the most attractive. A great deal of data confirms their efficacy for improving endothelial function and for reducing the incidence of such adverse events as death, unstable angina, MI, and the need for urgent revascularization. Other therapies (e.g., homocysteine lowering, estrogen therapy, and antioxidant therapy) improve endothelial function but there is little data to support their efficacy in reducing the adverse clinical events. Diet modification, smoking cessation, and regular exercise also improve endothelial function and should be recommended to all the patients who are at risk for atherosclerotic vascular disease.

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HERPES VIRUSES : NEWER PERSPECTIVES

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Introduction

About a decade back five human herpes viruses were known, but in the last 10 years three more new human herpes viruses have been described. These newer herpes viruses have been named human herpes viruses (HHV) 6, 7 and 8. On the basis of biological properties family herpesviridae is divided into three subfamilies.

Alphaherpesvirinae: They have short reproductive cycle, variable host range and rapidly spread in tissue culture causing destruction of host cells. Herpes simplex virus type 1 (HSV-1), herpes simplex virus type 2 (HSV-2), varicella zoster virus (VZV), equine herpes virus (EHV1) and pseudo rabies virus (RPV) belong to this subfamily.

Betaherpesvirinae: They have long reproductive cycle, restricted host range and infection progress slowly in tissue culture. In this subfamily cytomegalo virus (HCMV), human herpes virus 6 (HHV-6) and human herpes virus 7 (HHV-7) are included.

Gammaherpesvirinae: They have specificity for T or B lymphocytes and are latent usually in lymphoid tissue. Equine herpes virus 2 (EHV-2), Epstein Barr virus (EBV) and human herpes virus type 8 (HHV-8) are virus in this subfamily.

As mentioned above three new human herpes viruses has been added in the last 10 years and number has now reached upto eight. In this review only newer herpes viruses 6, 7 and 8 are described.

Human herpes virus 6 (HHV-6)

In 1986 Salahuddin and his colleagues reported the presence of novel virus in the peripheral blood lymphocytes of six patients with lymphoproliferative syndromes, two of them were also infected with HIV.[1] Based on its lymphotropism it was initially proposed to be a gammaherpesvirus, but its genetic similarity to human cytomegalovirus (HCMV) has led to its inclusion in the betaherpesvirinae subfamily. Molecular, structural and serological characterization confirmed it to be a herpes virus distinct from five known human herpes viruses.[2] The genome of this virus is a linear double stranded DNA molecule 160-170kb in size with a 67% homology with HCMV and 21% homology with other herpes viruses. One the basis of DNA restriction analysis, invitro tropism, use of monoclonal antibodies, HHV-6 can be separated in to two variants designated as variant A (HHV-6A) and variant B (HHV-6B).[3] Variant A is less frequently associated with clinical disease, however some reports shows increased association of this variant with HIV infection.[4] HHV-6B is more frequently isolated and has clear association with exanthem subitum.

HHV-6 appears to have an extensive host cell range. It can grow in $CD4^+$ cells,[5] to some extent in $CD8^+$ T cells, monocytes, natural killer cells, epithelial and brain derived cell.[6] The frequent detection of HHV-6 antigen in normal salivary glands,[7] lymphnodes,[8] neurons and glial cells of the brain suggests that virus can persistently infect cells or can establish latency and subsequently reactivate. The cellular receptor for HHV-6 is not yet known, however, it has been definitely proved not to be $CD4^+$ molecule.[10]

Most of the studies suggest a high seroprevalence of IgG antibodies to HHV-6 throughout the world[11] except in some areas of South-East Asia where a low seroprevalence is reported. Ninety percent of neonates are IgG positive probably reflecting passive transfer of maternal antibodies.[11] Prevalence drops at 4-6 months when maternal antibodies decline. IgM antibodies have also been found to increase in children age six months to one year. More than 90% of children become infected by first year of life and virtually 100% acquire infection by 3 years of age indicating clustering of primary infection in infants and toddlers.[12]

The route of transmission of HHV-6 is yet to be clearly identified, most children acquire infection through contact with secretions of adult caretakers shedding the virus in saliva.[7] Several recent reports suggest the possibility of vertical transmission as well.[13] Prenatal and intrauterine transmission of HHV-6 is strongly suggested but not proved.[14]

Symptomatic disease caused by HHV-6 occurs commonly in paediatric age group. HHV-6 has been definitely shown to be the causative agent of exanthem subitum or roseola infantum.[15] The variant B of HHV-6 is responsible for all cases of exanthem subitum.[16] The role of HHV-6 in central nervous system disorders has been considered but its wide distribution in brain tissue of normal

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people makes etiological role uncertain.[17] Other disease association in children include fever with otitis media, intussusception, hepatitis, haemophagocytic syndrome, lymphadenopathy and immune thrombocytopenic purpura. The risk of an adult acquiring HHV-6 disease is distinctly rare. However, when it does occur it usually takes the form of lymphadenopathy, heterophile negative infectious mononucleosis and hepatitis. Human herpes virus 6 (HHV-6) has also been implicated in necrotizing lymphadenitis (Kikuchi's disease) and sinus histocytosis with massive lymphadenopathy (Rosai-Dorfman disease) although its precise role in these conditions, if any, remain to be determined.

Reactivation of latent HHV-6 infection may occur after organ transplantation. The precise frequency of such episodes of viral reactivation depends on the type of organ transplant and degree of immunosupression. HHV-6 can cause both primary and recurrent infection in renal transplant recipients.[18] HHV-6 isolates recovered from bone marrow transplant (BMT) patients are always variant B.[19] The role of HHV-6 in liver transplantation is less well studied.

HHV-6 activates viruses like Epstein-Barr virus, cytomegalo virus, human papilloma virus[20] and has either an enhancing or suppressing action on replication of HIV.[21] It can induce $CD4^+$ molecule on mature lymphocytes and natural killer cell.[22,23] Such an event can make these cells potentially susceptible to HIV. Nevertheless, evidence of any pathogenic role of virus in enhancing the progression to AIDS has not been conclusive.

Detection of IgM antibodies is a reliable maker of primary infection in children but not in adults as IgM increases in reactivation. In general a four fold or greater rise in anti-HHV-6 antibody titre between acute and convalescent serum sample suggest active replication. The virus can be cultured in lymphoblastoid cell live. Detection of HHV-6 DNA in cell free plasma specimens also suggest the presence of active HHV-6 replication.

Considering the ubiquity of the organism its acquisition in childhood and lack of an effective vaccine, prevention of primary HHV-6 infection is not feasible. However, reactivation may be prevented by antiviral prophylaxis. The drugs active against HHV-6 include gancyclovir and foscarnet. In vitro studies has demonstrated that cidofovir is also active against HHV-6. Although acyclovir is also inhibitory to HHV-6, it is less active than gancyclovir and foscarnet.

Human herpes virus 7 (HHV-7)

In 1990 Frenkel et al isolated a previously unrecognized human herpes virus from $CD4^+$ T cell purified from peripheral blood lymphocytes of a healthy individual.[24] The 145kb genome of HHV-7 shows homology to CMV and HHV-6 therefore this virus was placed in betaherpesvirinae.[25] The virus was however distinct from herpes simplex virus, varicella zoster virus, Epstein Barr virus and cytomegalo virus.

HHV-7 like HHV-6 grows well in $CD4^+$ lymphocytes. It grows best in cord blood lymphocytes and in established T-cell lines. The virus is more cell associated, less cytopathic and grows with slower kinetics in culture than HHV-6.[26] HHV-7 unlike HHV-6 appears to utilize $CD4^+$ molecule for its receptor. HHV-7 also down modulates expression of $CD4^+$ molecule, hence the role of its envelope in anti HIV therapy has been proposed.[27]

Human herpes virus 7 has yet to be definitively shown to cause specific disease. However, data suggests its association with first and second episode of exanthem subitum, fibrile seizures, haemophagocytic syndrome.[28] The knowledge about HHV-7 is till limited as compared to HHV-6, however latency is well known in this virus. Further studies might well reveal some more pathogenic association.

Primary HHV-7 infection usually occurs within first five years of life, although the age at which infection occur appears to be some what later than early age documented for HHV-6. Most adults have serological evidence of prior HHV-7 infection. The major reservoir for HHV-7 remains to be proved. The HHV-7 DNA has been detected by PCR from salivary glands thus suggesting that salivary glands may be the site of viral replication and transmission.[29] HHV-7 DNA has also been detected in cervical swabs of pregnant women raising the possibility of perinatal or congenital transmission of HHV-7 as well.[30]

Diagnosis required the detection of virus, viral antigen or viral nucleic acid. Viral antigen can be detected by immunological assay using HHV-7 specific monoclonal antibodies. Serological assay has yet to be standardized. Recombinant antigen based serological assays will probably overcome issue of cross reactivity and the high seroprevalence rate in the population.

Human herpes virus 8 (HHV-8)

HHV-8 was discovered by Chang et al using novel molecular approach.[31] DNA sequence in Kaposi's Sarcoma lesions were compared with those of normal skin and unique DNA sequences were identified that were closely related to region of the genomes of herpes virus Saimiri and Epstein Barr virus. The herpes virus like sequences are found in all forms of Kaposi's sarcoma from various parts of world whether the patients are infected with HIV or not.[32] Similar sequences were also detected in B-cell lymphoma in abdominal cavity.[33] HHV-8 is a member of gammaherpesvirinae subfamily, since it infect lymphocytes and is associated with cell immortalization and transformation. The HHV-8 genome is 170kb in size and sequence resemble to those of cyclin D, a cell cycle

inducer.[34] HHV-8 RNA transcripts have been found in endothelial cells of Kaposi's sarcoma lesions and in peripheral blood monocytes.[35] These data suggest replication in vivo of HHV-8 in some cells of Kaposi's sarcoma tumor and mononuclear cells.

In contrast to HHV-6 and 7 replication of HHV-8 in conventional cell has not been achieved. However, human papilloma virus (HPV) transformed endothelial cell line BB19 and adenovirus transformed human kidney epithelial cell line 293 have shown potential susceptibility to HHV-8.[36] The virus does not replicate in conventional cell line which is major hindrance to study the characters of this virus.

The finding of HHV-8 virus and DNA sequence by in situ hybridization in endothelial cells and spindle cell suggests its association with Kaposi's sarcoma. Possible role of HHV-8 in endothelial derived cancers such as angiosarcomas and in angiolymphoid hyperplasia needs to be further evaluated. The detection of HHV-8 DNA in body cavity B-cell lymphoma suggests that this agent may be involved in transformation process. The role of HHV-8 in lymphoproliferative syndrome and multicentric Castleman's disease has been proposed.[37] Serological studies have revealed a strong corelation between antibodies to HHV-8 and the presence of Kaposi's sarcoma or B-cell lymphoma in abdominal cavity.[37] The detection of HHV-8 virion in saliva samples suggest that salivary contact could contribute to HHV-8 transmission.[38] The occasional detection of HHV-8 DNA in semen samples from Kaposi's sarcoma patients indicate that this agent may be sexually transmitted.[39] The distribution of virus resemble herpes simplex virus type 2 which is also sexually transmitted. A higher sero-positivity in homosexual men and not in women infected with HIV supports the role of receptive anal intercourse as a major infective mechanism. Thus HHV-8 resembles Epstein-Barr virus in its tropism and latency in B lymphocytes while resembling HSV-2 in its epidemiology.

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CEREBRAL PALSY

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Introduction:

Cerebral Palsy (CP) is a kind of physical (motor) impairment caused by a non progressive brain disorder which presents in the early childhood with delayed development, abnormal posture and movement. CP results from a wide variety of pathological events and may be accompanied by visual, hearing, and sensory defects, seizures, and mental retardation.

Epidemiology:

The correct epidemiological assessments are difficult to ascertain as mild cases are likely to be missed during surveys, so the prevalence of CP may well be higher than what has been reported in various studies. According to the conservative estimates, prevalence rate of CP is around 10-14 per thousand which is very high as compared to what is seen in the developed world where its prevalence is 2-4/1000 in school age children. Studies assessing the actual prevalence in developing countries are required.

Classification:

The most commonly used classification is the clinical classification, which is based on the physiological and topographic features of the palsy and its predominant patterns are spastic, dyskinetic, ataxic and atonic however mixed features are seen in some patients and some cases remain unclassified. Spastic CP results from the involvement of the upper- motor neuron of the pyramidal system which may affect only one side of the body, hemiplegic CP, both sides of the body with greater involvement of legs than arms, diplegic, or all the four limbs equally, tetraplegic or quadriplegic, besides there can be monoplegia, triplegia or double hemiplegia. This topography depends upon the location of the lesion in the brain. dyskinetic.CP results from the involvement of the extrapyramidal system, typically the basal ganglia and these children usually have fluctuating dystonia. Ataxic CP results from involvement of the cerebellum. As the central nervous system and locomotor system mature the outward motor manifestations of a static lesion change.

Pathophysiology:

Pathophysiological process resulting in the cerebral palsy may occur in the antenatal, perinated or postnatal period or a combinatio i thereof.

Antenatal:

Genetic syndromes may present with CP, particularly of diplegic and ataxic types especially where consanguineal marriage patterns are practised. Neuronal migration defects, due to the failure of the normal process of migration of nerve cells from their periventrianlar site of origin to the cortex during second trimester may underlie the CP of any type. Vascular lesions of the developing brain may result in ischemic necrosis and porencephalic cysts leading to cerebral palsy. Intrauterine infections like rubella, cytomegalovirus and toxoplasmosis also can result in CP Maternal micronutrient deficiency during pregnancy can lead to cerebral palsy in the baby.

Perinatal:

Asphyxia explains 10-20 percent of the CP in west while as it is responsible for nearly 40 percent of CP in developing countries out of which some have an underlying predisposing factor. Manifestation of the hypoxic ischemic encephalopathy in the newborn baby suggests the occurance of significant perinatal/ birth asphyxia. Perinatal asphyxia can lead to any type of CP, but usually the lesions tend to be widespread and severe resulting either in dyskinetic CP or tetraplegic CP with microcephaly and other associated impairments.

Uuconjugated hyperbilirubinemia in sick neonates results in kernicterus and presents as dyskinetic CP, initially as dystonic type before progressing to classical choreoathetoid pattern towards school age. Perinatal infections, (neonatal meningitis) and the intracranial hemorrhage of the newborn (preterm) are the other important causes.

Postnatal:-

Postnatal causes usually refer to the insults causing brain damage between one month and one year of age. Severe

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dehydration in diarrhoeal diseases and hypoxia in respiratory diseases are not uncommon causes of CP. Infections meningitis, encephalitis, and head injury are the other causes of cerebral palsy in developing world.

Assessment of the Child with CP

Diagnosis is made from the careful history and clinical examination family history and careful search for dysmorphic stigmata will lead to the evidence of genetic cause. Immediate postnatal history of sucking, crying, body posture, movements, convulsions is an important clue maker. The normal early developmental history followed by a major illness should suggest a postnatal cause and a deteriorating developmental picture should alert the clinician to the possibility of a progressive degenerative process which is not the CP.

Among the diagnostic testing baby is subjected to thyroid testing, genetic testing, chromosomal analysis, imaging proceedures and some enzyme studies for metabolic disorders. Though these proceedures are a costly affair for the communities of the developing world so the limited resources are better utilized for therapeutic input.

The child needs to be assessed for its extent of disability. The child should be observed during his/her routine activity for the presence of secondary complications, (such as contractures and bony deformities and dislocations). Also the child should be observed for the associated impairment of vision, hearing, sensation and cognition. A developmental screen appropriate for a community should be developed.

Management:

Before proceeding with the actual management it is professional obligation of the physician to discuss, the importance & impacts of management therapy, with the patient. If genetic aetiology is suspected then counseling is an important issue.

Another aspect of the management is the rehabilitation therapy which is provided by the various government and non-governmental organization operating at various levels of the society. Now-a-days community based physical & mental rehabilitation centres are rendering these services with the active involvement of the family members of the disabled child.

Medical Treatment:

Medical treatment is selected according to the type of involvement and clinical manifestations i.e. cerebral irritability and restlessness and sleeplessness are treated with chlorpromazine, excessive hypertonicity is treated with baclofen and benzodiazepines. Seizures are treated with anticonvulsant. A variety of brain tonics are yet under evaluation. Selective rhizotomy is done for the permanent relief of the persistent painful hypertonia. Tender contractures are relieved by surgical sectioning of the tendons (tenotomy)

Prevention.

Most important aspect for the prevention of CP in developing countries is maternal health education, improvement of the maternal health and provision of Antenatal and perinatal services for monitoring the pregnancy, progression of labour and the baby during the newborn period, and providing the intervention and correction wherever required. Thereafter diagnostic promptness and early management of meningitis, encephalitis, metabolic encephalopathies and the conditions like dehydration, respiratory problems likely to give rise to hypoxia, go a long way in the prevention of CP.

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LABOUR EPIDURAL ANALGESIA, ITS EFFECTS ON NEWBORN BABIES: A COMPARISON OF TWO TECHNIQUES.

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Abstract: Labour is a painful process in women and pain relief is essential for the well being of both the mother and the fetus. In a randomized double blind study 60 ASA I primiparas, between the age group of 20-28 years were divided into two groups (group I and II respectively) of 30 each to study the effect of two different techniques of lumbarepidural analgesia and its effect on the newborn babies. Lumbar epidural block was established in both the groups with subsequent administration of 4ml of lidocaine 1% with adrenaline (1:200,000) "on-demand only" in group I and 'at regular intervals" of 110 mins in group II, throughout labour. Latency of onset of analgesia duration of analgesia, % motor blockade and APGAR score of the newborn were noted a regular intervals. A note was made about the mode of delivery. The quality and continuity if analgesia was found to be better in group II, although with a higher incidence of instrumental deliveries and maternal complications (urinary retention, hypotension) in the same group. There was no difference between the two gruops as far as motor blockade was concerned. Fetal well being assessed by APGAR score at 1 and 5mins was unaffected by the technique used to administer the incremental doses in the present study. It was concluded that epidural analgesia provides a very good pain relief in labour without having any adverse effects on the well being of the newborn.

Keywords: Labour, Epidural, Lignocaine, APGAR Score.

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INTRODUCTION

Labour is a painful process in women and in primigravida the pain is far in excess of their expectations. Pain relief in labour is essential for the well being of both mother and the fetus. In western countries analgesia in labour is not only accepted as necessary but is also demanded as a right by women. Among regional analgesia techniques used for labour, extradural analgesia is widely accepted and is most effective and reliable method of pain relief[1]. Lumbar extradural block in labour was first given in 1935 by Graffagnio and Seylor while first continuous extradural block in labour was given by Flower's et al in 1949. The technique is claimed to have beneficial effects on fetus as well as on the mother during and after labour.

Extradural block in labour is produced in two ways

1. By regular administration of incremental doses of local analgesic given at suitably timed intervals i.e., regular top-up technique.
2. By intermittent injection of local analgesic i.e., on-demand top-up technique.

Bromage claimed that reduced total dose of local analgesic is needed with intermittent technique. The disadvantage associated with this intermittent technique is that the patient may experience some pain in the interanalgesic interval and when lignocaine is used as a local analgesic, the interanalgesic intervals may encourage the development of tachyphylaxis[2].

Regular top-up technique (continuous extra dural blockade) avoids tachyphylaxis and provides a greater patient satisfaction[3]. This technique is associated with administration of greater dose of local anaesthetic compared to the intermittent technique, with the result that there is increased degree of motor and sensory blockade and increased incidence of 'operative deliveries'.

MATERIAL AND METHODS

We studied 60 ASA-I primiparas between the age range of 20 – 28 years. An informed consent was taken from each patient, after explaining the procedure. Patients with infection at the site of proposed injection, coagulation defects, hypovolemia and hypotension i.e. systolic pressure < 90 mm Hg, contracted pelvis, spinal deformity, pre-existing neurological disorders and patients on anticoagulant therapy were excluded from the study.

All the patients were weighed beforehand and reassured about the procedure. Intravenous infusion of crystalloid

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(Dextrose 5%) was instituted in every patient. Infusions containing uterine stimulants were stopped temporarily at the time of performing the extradural block as these drugs by way of increasing the severity of uterine contractions, increase the intensity of labour pains and can thus render the patient uncooperative.

Extradural injection was performed only after establishment of labour i.e. uterine contractions occurring, in a regular pattern, after every 3- 5 minutes.

Pain score was assessed on a four point scale, immediately before, and thirty minutes after each extradural injection with 0 as no pain; 1 as discomfort; 2 as moderate abdominal pain; and 3 as severe abdominal pain.

TECHNIQUE

Epidural block was performed under strict aseptic precautions with the patient in left lateral position. Skin and subcutaneous tissue, at the level of L2 –L3, were anesthetized with 1% lidocaine using a 25 Gauge needle. Next, a 16 Gauge Touhy needle was introduced through the L2-L3 interspace. The needle was advanced with the bevel facing upwards; the epidural space was identified by the loss of resistance technique. Afterwards, epidural catheter was advanced into the epidural space. The Touhy needle was withdrawn after advancing the epidural catheter 3-5 cms into the epidural space. The area of skin puncture was sealed by antiseptic dressing and epidural catheter was fixed in the left mammary region of the patient. 3 ml of 1% lidocaine with adrenaline (1;200,000) was injected as a test dose into the epidural space through the epidural catheter, watching for any untoward effects for a period of 5 minutes. Loss of motor power, especially in the feet was sought, so as to exclude the subarachnoid administration. This was followed by administration of 7ml of 1% lidocaine with adrenaline (1: 200,000) through the catheter.

Lateral position was maintained by turning the patient from side to side every 5-10 minutes, after the injection. The patient was never kept supine. Left lateral tilt was given when the patient was to be placed in lithotomy position, to avoid aortocaval compression. Drug used throughout the study was lidocaine 1% with adrenaline 1:200,000. Regarding the mode of administration , patients were divided into two groups of 30 patients each as under:-

Group I received 4ml of lidocaine 1% with adrenaline (1:200,000) on demand only (i.e. when blockade had diminished and contractions had become painful) throughout labour.

Group II received the same dose of local anesthetic (i.e. 4ml of lidocaine with adrenaline 1:200,000) at 110 minutes intervals throughout the labour.

During second stage of labour, the two groups of patients did not differ from each other, as far as mode of administration of local anesthetic was concerned. Both the groups received the same amount of the drug, while keeping the patients in the sitting position for 3-5 minutes.

After establishment of extradural blockade following parameters were recorded :-

1. Time of onset of blockade i.e. the time (in minutes) from injection to the first contraction described by the patient as 'not painful'.
2. Motor blockade of legs measured on a five point scale as under:-
   0-Patients having total paralysis (i.e. unable to move lower limbs)
   I-Patient can move legs in horizontal plane only.
   II-Patient can raise legs against gravity but not against resistance
   III-Patient having a slightly reduced power but can still raise against gravity and resistance .
   IV-Patient having normal power.

Motor blockade was tested at intervals of 30 mins after each injection .

3. Total bolus dose : Total on demand dose and total dose of lidocaine used in each patient was also noted.
4. Mode of delivery i.e. a) Spontaneous vaginal delivery –SVD , b) Forceps delivery –FD , c) Vacuum Assisted Delivery –V.D , d) Cesarean Delivery –CD , was also noted .
5. Any maternal complications as a result of epidural blockade and the treatment given were also recorded.
6. APGAR score : was noted by assessing the APGAR score at one and five minute intervals following delivery.
7. Grading pain after the epidural blockade in the post delivery period as follows 1 – No Pain , 2 – Slight Pain, 3 - Bearable Pain, 4 - Unbearable Pain.
   The relevant observations were evaluated statistically.

Table-1: Distribution of age and weight in two groups.

	Group I	Group II
Age; years, mean (SD)	23.73±2.32	22.83±2.32
Weight; kg, mean (SD)	52.84±1.86	53.81±2.07

Table-2: Comparison o mean pain score before epidural and 30 min after each epidural

	Group I	Group II	Statistical significance
Before epidural	2.93±0.25	2.90±0.30	N/S
30 min after			
Ist injection	0	0	N/S
2nd injection	0	0	N/S
3rd injection	0	0	N/S
4th injection	0.16±0.36	0	S(p<0.01)
5th injection	0.30±0.46	0	S(p<0.01)

Table-3: Comparison of mean time of onset of analgesia (in minutes) in two groups

Observation	Group I	Group II
Mean time of onset of analgesia	11.33±0.87	10.83±1.04

The result was statistically significant with p-value of <0.025

Table-4: Comparison of mean total dose of lignocaine (in mgs) used in two groups

Observation	Group I	Group II
Mean total dose of lignocaine) (in mgs	235.72±44.66	249.92±44.55

The result was statistically insignificant with p-value of <0.20

Table-5: Comparison of maternal complications in two groups.

Complication	Group I	Group II	Statistical significance
Urinary retention	4(13.3%)	5(16.6%)	N/S
Hypotension	2(6.6%)	4(13.33%)	S

There was statistically significant difference in the incidence of hypotension between the two groups.

Table-6: Comparison of mean grade of pain post-delivery in two groups.

Observation	Group I	Group II
Mean grade of pain	170±0.59	1.13±0.34

The result was statistically significant with p-value of <0.0005.

Table-7: Comparison of worst pain experienced, in two groups.

Group	No pain	Slight pain	Bearable pain	Unbearable pain
I	11(36.3%)	17(56.6%)	2(6.6%)	—
II	26(86.6%)	4(13.3%)	—	—

Table-8: Comparison of muscle power 30 min after each epidural administration.

	Group I		Group II	
	Grade III	Grade IV	Grade III	Grade IV
30 min after				
Ist injection	7(23.33%)	23(76.66%)	8(76.66%)	22(73.33%)
2nd injection	5(16.66%)	25(83.33%)	9(30%)	21(70%)
3rd injection	5(17.24%)	24(82.75%)	9(31.03%)	20(68.96%)
4th injection	3(15.87%)	16(84.21%)	8(36.66%)	14(63.63%)
5th injection	2(20%)	8(80%)	6(42.85%)	8(57.14%)

Table-9: Comparison of apgar score of newborn babies one minute after deliver in two groups.

	8	9
Group I	10(33.33%)	20(66.66%)
Group II	6(20%)	24(80%)

Results

The two groups were comparble with regards to age and weight with mean age 23.73±2.32 in group I and 22.83±2.32 in group II, and mean weight of 52.84±1.86 in group I and 53.81±2.07 in group II respectively (Table I).

The mean pain score was 2.93±0.25 in group I while it was 2.90±0.30 in group II. The two groups showed an insignificant statistical difference between them as far as pain score was concerned before initiating epidural block (p,0.25). Pain score was again assessed 30 minues after the first, second and third epidural injection in both the groups. Pain score was "0" in both the groups. Pain score 30 minutes after the fourth and fifth injection in group I was 0.16±0.36 and 0.30±0.46, whereas in group II pain score 30 minutes after the fourth and fifth injection was "0" with statistical analysis revealing a significant difference in pain scores between the two groups after the fourth and fifth injection (Table 2).

The mean time of onset of analgesia was 11.33±0.87 min in group I and 10.83±1.04 in group II respectively with ap-value of <0.025 (Table 3).

The mean total dose of lignocaine used in group I was 235.72±44.66 mgs whereas in group II it was 249.92±48.55 mgs. The two groups showed an insignificant statistical difference in this regard with p-value of <0.20 (Table 4)

In group I 27 (90%) patients delivered spontaneously while as 3(10%) patients were delivered by ventouse. In group II 25 (83.33%) patients delivered spontaneously and 5(16.66%) patients were delivered by ventouse. Thus more number of patients required delivery by instrumentation (ventouse) in group II and the two groups showed a significant statistical difference from each other (p<0.0005).

Urinary retention was noted in 4(13.33%) patients in group I and in 5 (16.66%) patients in group II. There was an insignificant statistical difference difference between the two groups with p-value of <0.10. Hypotension was observed in 2(66.6%) patients in group I and in 4 (13.33%) patients in group II. The two groups showed a significant statistical difference from each other with p-value of 0.0005 (Table 5).

Post-delivery interview revealed mean pain grade of 1.70±0.59 in group I while in group II it was 1.13±0.34 in group II and the result was statistically significantly with p-value of <0.0005 (Table 6).

In group I, 36.3% patients had no pain and in group II 86.6% patients had no pain throughout epidural. Slight pain was recorded in group I in 56.6% of patients and in 13.3% of patients in group II. Bearable pain was recorded in 6.65% patients in group I whereas no patient in group II had bearable pain. Unbearable pain was not recorded in any patient of either groups (Table 7).

In group I the muscle power was grade III in 7(23.33%) patients and grade IV in 23 (76.66%) patients while in group II grade III power was present in 8 (26.66%) patients and grade IV power was present in 22(73.33%) patients 30 min after Ist injection. The muscle power was grade III in 5 (16.66%) patients and grade IV in 25983.33%) patients of group I, and grade III in 9(30%) and grade IV in 21 (70%) patients 30 min after 2nd injection. The muscl-

power was grade III in 3 (17.24%) patients and grade IV in 24(82.75) patients of group I, and grade III in 9(31.03%) and grade IV in 20(68,96%) patients 30 min after 3rd injection. In group I the muscle power was grade III in 3(15.78%) patients and grade IV in 16(84.21%) patients whereas in group II grade III power was present in 8(36.36%) patients and grade IV power was present in 14(63.63%) patients 30 min after 4th injection. In group I grade III muscle power was present in 2(20%) patients and grade IV in 8(80%) patients whereas in group II grade III muscle power was present in 6(42.85%) patients and grade IV in 8(57.14%) patients (Table 8).

At one minute the apgar score was 8 in 10(33.33%) newborns and 9 in 20(66.66%) newborns in group I, and in group II it was 8 in 6 (Table 9). (20%) newborns and 9 in 24(80%) newborns. At five minutes the apgar score was 10 in all the 30 newborns of group I and in all the 30 newborns of group II also.

DISCUSSION

Labour is a painful process. The pain if permitted to become more than a little obtrusive prompts a series of metabolic responses in the mother, which are finally reflected in the fetus. These include a progressive increase in metabolic acidosis[4], an increase in the concentration of plasma cortisol[5], and an increase in the concentration of catecholamines[6]. Unrelieved pain of labour may also result in hyperventilation and the resultant hypocapnia can be severe enough to produce tetany[7], and reduces the uteroplacental blood flow by upto 25%. The respiratory alkalosis further impairs feto-maternal gas exchange by shifting the oxyhemoglobin dissociation curve to the left and fetal pao may fall by upto 23%[8]. Effective pain relief reduces plasma noradrenaline concentrations[9], prevents metabolic acidosis[10], and decreases maternal oxygen consumption by upto 14%[11].

The present study was aimed to evaluate the effectiveness of epidural analgesia in abolishing the pain of labour and also to compare between regular 'top-ups' and 'on demand' epidural injections for labour analgesia.

Pain score prior to epidural blockade as assessed on a four point scale using the method described by Purdy et al[3] revealed a pain score of 2.90 ± 0.30 in groupl and 2.93 ± 0.25 in group II. It is evident that mother in labour have very high pain score and therefore must receive some form of pain relief. Pain relief produced by epidural blockade as evaluated by assessing the pain score at 30 minute interval following each epidural injection revealed complete pain relief in both groups after 1st, 2nd and 3rd injections with '0' pain score in both the groups. 30 minutes after 4th and 5th injections a significant difference in pain scores was seen between the two groups with pain score of 0.16 ± 0.36 (4th injection) and 0.30 ± 0.46 (5th injection) in group I patients, and '0' pain score in group II patients. Thus continuity of analgesia was better in the group which received regular 'top-ups'. Similar observations have been made by purdy et al[3].

The mean total dose of lignocaine was 235.72 ± 44.66mgs in group I and 249.92 ± 48.55mgs in group II. No tachyphylaxis was observed in patients of either group. Bromage suggested that small doses do not provoke an appreciable degree of tachyphylaxis and potency does not diminish after 7 or 8 maintenance doses during a 12- 14 hour period of analgesia.

A slightly higher incidence of ventouse delivery was observed in group II compared to group I. This could be due to a higher degree of motor blockade produced by regular top-ups in the study by Purdy[3] the mode of delivery was unaffected by the technique used. The incidence of instrumental delivery following epidural analgesia was reported as 35% by Fredrick et al, 89% by Bromage[12], 60.6% by Crawford[13] and 27% by Romino[14]. The incidence of instrumental deliveries in the present study was 10%.

13.33% patients in group I required cathetrisation for urinary retention in group I whereas 16.66% patients in group II required cathetrisation for urinary retention. The cause for urinary retention is extensive motor weakness produced by epidural blockade. Brownridge[1] reported 10% incidence of urinary retention in his study. Higher incidence of hypotension (13.33%) was observed in group II compared to group I (6.6%). Purdy et al[3] in his study reported 4.5% incidence of hypotension in top-up group and only 2.5% in on-demand group.

In the regular top-up group (group II) there was a significantly better quality of analgesia in the post delivery period compared to that of group I. Similar observations were made by Purdy et al[3] in his study.

In the present study there were no differences between the two groups as far as motor blockade was concerned. The observation goes well in agreement with that of Purdy et al[3]. According to Bromage et al [12] the concentration of lignocaine will govern to a large extent the accuracy with which analgesia can be restricted to the painful segments and these authors have suggested that when accuracy is technically impossible it is safer to use relatively larger volumes of a dilute solution e.g., 0.8-1.0% solution of lignocaine, since motor power is not much affected by this concentration.

Fetal well-being assessed by apgar scores at 1 and 5 minutes was unaffected by the technique used to administer the incremental doses in the present study. Similar observations have been made by other authors also, viz., Wingate et al[15], Moir et al[16], and chouhan et al[17].

CONCLUSION

Epidural analgesia provides a very good pain relief for

labour pains as is evident from our study, without having any adverse effects on the well being of newborn babies. The quality and continuity of analgesia provided by regular "top-ups" is definitely superior to the "on- demand" injections for epidural analgesia.

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ROLE OF FESS IN HEADACHE

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Abstract: *Headache is one of the commonest maladies, which affects humans. It is quite perplexing both for the patients as well as the clinicians. Headache can have either a clear rhinogenic cause or a clear non-rhinogenic medical cause. Very small anatomical or pathological changes in osteometal complex area or lateral nasal wall can produce quite-disturbing symptoms. These small changes are usually missed on clinical examination and conventional radiographic examination. C.T. Scan osteometal complex with coronal cuts combined with nasal endoscopic examination reveal remarkable information about the cause of Headache. Small polyps or contact areas produce pressure changes, which cause release of neuropeptides leading to pain. In this study 40 patients were evaluated. Choncha bullosa, anatomical variations, post-septal deviations, small polypi in OMC area and contact areas in OMC area were found to be the major causes of headache. Minor surgical endoscopic operations gave nice results 25% improvement was seen in 3% patients, 50% improvement in 8% patients and 75% improvement in 50% patients and more than 75% improvement was seen in 39% of patients who were labeled a cured.*

Key words: *Headache Osteomeatal complex Nasal Endoscopy.*

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Introduction:

Headache is a perplexing condition which annoys the patient and presents a diagnostic challenge to the clinician. Since the causes of headache are quite varied viz; medical, neurological, ophthalmological, otolaryngeological and psychiatric, the patient many times does not land the proper place. In general hospital practice, headache patient first goes to an internist. The blood pressure, B.P. being normal the internist refers the patient to the ophthalmologist, vision being 6/6 (normal), he refers the patient to the otolaryngologist who reports anterior & posterior rhinscopy as normal and the patient finally gets lost, may land with the psychiatrist. There is strong need for the integrated & coordinated team work for headache patients preferably under one roof - The Headache - Clinic.

The otolaryngologists have to realise their role in the management of substantial percentage of these headache patients. Stammberger (1988) did the pioneering work in evaluating the role of nasal endoscopy in headache patients. He observed that the otolaryngologist is confronted with three different groups of headache patients:

1. Those with clear rhinogenic cause which may be anatomical, inflammatory, traumatic or neoplastic.
2. Those with clear non-rhinogenic cause like migraine, neuralgias, high/low BP, ophthalmic causes, neurological and other medical causes.
3. Those headache patients who neither have clear rhinogenic cause nor have clear non-rhinogenic cause. It is this group of patients that can present a very rewarding challenge for the nasal endoscopist.

For the present study we have selected 40 patients of headache who belonged to the third group i.e., having neither clear rhinogenic cause of headache nor clear non-rhinogenic cause of headache. The endoscopic rhinogenic causes otherwise hidden on anterior & posterior rhimoscopy & conventional radiography are evaluated, the role of C.T. Scan in such cases is discussed & the role of endoscopic surgical procedures in the management of headache is also evaluated.

Material & Methods:

Patients of headache attending the ENT OPD of our hospital were screened from February 1, 2000 to September 30, 2000. Patients having clear rhinogenic cause like DNS, gross polyposis seen on anterior or posterior rhinoscopy & frank purulent sinusitis were excluded. Patients having clear medical cause of headache like migraine, hypertension, neuralgias, cervical spine disorders, TMT problems, ophthalmic causes, allergies or other neuro-causes were also excluded from this study. Children below age 14 years were also excluded. the criteria for selection of patients was:

Headache as the chief complaint, anterior rhinoscopy, posterior rhinoscopy, sinus radiographs & cervical spine radiographs reported as NAD. Examination by ophthalmologist, Dentist, Internist and others also reported as normal. With this criteria of selection & exclusion 40 Patients were selected for the present study. Coronal C.T.

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Scan with 5 mm cuts at osteomeatal junction was advised in most of the patients but it was not possible in all cases as some patients could not afford it. Most of the cases were done in local anaesthesia but some cases were done in G.A. as well. 0° 4mm rigid nasal endoscope was mainly used. Surgical procedures ranged from minor endoscopic surgical procedures like partial turbinectomy, conchoplasty, infundibulotomy to anterior ethmoid clearance, total anterior and posterior ethmoid clearance, frontal recess clearance, sphenoidotomy and septal correcton which included localised endoscopic correction in some cases & complete septoplasty in some cases.

Procedures performed

Procedure	Unilateral	Bilateral	Total
1. Uncinectomies & Infundibulotomy	15	25	40
2. Ant. Ethmoidectomy	12	20	32
3. Total Ethmoidectomy	11	2	13
4. M. Meatal Meatotomy	16	4	23
5. Sphenoidotomy	9	3	12
6. Frontal Sinus Expl.	4	2	6
7. Conchoplasty	11	3	14
8. Partial M. Turbinectomy	10	15	25
9. Septoplasty			11

Results:

There were 27 males and 13 females with age ranging from 15 years to 70 years with maximum no. of patients in 2nd to 4th decade.

Site of headache was global in 30% frontomaxillary in 15%, maxillary in 12.5%, mid-canthal in 15%, peri-orbital in 5%, retro-orbital in 7.5%, vertex in 10% & temporal in 5%. Severity of headache was mild in 20%, moderate in 45%, moderately severe in 22.5%, severe in 10% and acute in one patient (2.5%).

Endoscopy Findings:

Variations of Uncinate Process

Variation	Unilateral		Bilateral	
	No. of Patients	% of Patients	No. of Patients	% of Patients
Hypertrophied	11	27.5	04	10
Medially Crved	05	12.5	—	—
Contacting Middle Turbinate	06	15	01	2.5

Variations of Bulla ethmoidalis

Variation	Unilateral		Bilateral	
	No. of Patients	% of Patients	No. of Patients	% of Patients
Hypertrophied	12	20	04	10
Contacting Middle Turbinate	07	17.5	01	2.5

Concha Bullosa

Side	No. of Patients	% of Patients
Unilateral	11	27.5
Bilateral	03	7.5

Posterior Deviation of Septum

No. of Patients	% of Patients
11	27.5

Middle Turbinate

Variation	Unilateral		Bilateral	
	No. of Patients	% of Patients	No. of Patients	% of Patients
Hypertrophide	05	12.5	08	20
Contact Area with Septum	05	12.5	07	17.5

Condition of Anterior Ethmoid Cells

Abnormality Seen	Unilateral		Bilateral	
	No. of Patients	% of Patients	No. of Patients	% of Patients
Mucosal Thickening	08	20	16	40
Polypoidal Change	04	10	04	10

Condition of Posterior Ethmoid Cells

Abnormality Seen	Unilateral		Bilateral	
	No. of Patients	% of Patients	No. of Patients	% of Patients
Mucosal Thickening	08	20	02	05
Polypoidal Change	03	7.5	—	—

Maxillary Sinus Involvement

Abnormality Seen	Unilateral		Bilateral	
	No. of Patients	% of Patients	No. of Patients	% of Patients
Mucosal Thickening	10	25	07	17.5
Polypodial Change	06	15	—	—

Sphenoid Sinus Involvement

Unilateral		Bilateral	
No. of Patients	% of Patients	No. of Patients	% of Patients
09	22.5	03	7.5

Fronto Ethmoid Recess

Abnormality	Unilateral		Bilateral	
	No. of Patients	% of Patients	No. of Patients	% of Patients
Mucosal Disease	08	20	02	05
Polypodial Change	04	10	02	05

Frontal Sinus Involvement			
Unilateral		Bilateral	
No. of Patients	% of Patients	No. of Patients	% of Patients
04	10	02	05

Result of Present Study		
Result	Subjective Improvement of Symptoms %	% of Patient
Worsened	—	Unchanged
Slight Improvement	25	03
Improved but needed Some additional Treatment	50	08
Improved, needed no Treatment	75	50
Cured	>75	39

Case Reports:

Case I

A 60 year old male presented with acute severe headache mimicking some cerebrovascular accident. Patient was tossing with severe pain which was global in distribution and constant in nature. Medical, neurological & ophthalmological examination was normal. Anterior rhinoscopy & posterior rhinoscopy also did not reveal anything. Nasal endoscopy was done straight away as patient had severe pain. It revealed very large, highly inflammed angry red looking middle turbinate which was crushed. Patient was absolutely pain-free in the evening.

Case II

A 55 year old male, professor of English by profession, presented with headache of long duration. There was no associaed nasal obstruction or nasal discharge. Anterior & posterior rhinoscopy again was un-informative. Examination by Internist, Dentist, Ophthalmologist & Neurologist was reported as normal. Coronal CT of OMC was done which revealed hypertrophied uncinate process with large bulla having close contact with M. turbinate, thus blocking the osteomeatal area on right side and posterior septal deviation on left side with ethmoid cloudiness. Infundibulotomy & anterior ethmoid clearance was done on right side. headache improved on right side alone & persisted on left side. Septal correction & anterior ethmoid clearance with M. meatal meatotomy was done on left side after three weeks & headache on left side also improved. Patient is headache free as seen last at six month follow up.

Case III:

A 25 year old male had undergone septoplasty at All India Institute of Medical Sciences New Delhi but his main symptom of headache continued. He reported to our OPD. A coronal CT of OMC area was advised which showed enlarged bulla ethmoidalis with ethmoid disease on right side with complete block of osteomeatal area & ethmoid & maxillary sinus disease on the left side. Anterior ethmoid clearance was done on both sides with M. Meatal meatotomy & maxillary sinus clearance on left side. Patient is headache free when last seen after 8 months after surgery.

Discussion

Nasal endoscopy has provided new horizons and new challenges to the otolaryngologist. Nasal endoscopy combined with coronal CT has made the approach to Sino-nasal disease more scientific, rational and accurate. Before these two modalities the understanding of the pathophysiology of Sino-nasal system and subsequent management was quite crude & more imaginative than real. We now realise that many septoplasties being done without the aid of prior nasal endoscopic & CT evaluation are un-indicated. Minor OMC problems, which produce quite troublesome symptoms like Concha bullosa, variations in uncinate process, agger nasi & ethmoidal bulla, remain hidden without the aid of CT Scan & Nasal endoscopy. These patients were being subjected to septal surgeries unnecessarily. This is about the role of nasal endoscopy & coronal CT in general, but these two modalities have a highly significant role in the diagnosis and management of those headache patients who do not have either clear rhinogenic or non-rhinogenic medical cause of headache.

Sluder[1], as early as 1927, suggested the relation between headache and negative pressure. It was McAuliffe[2] (1943) who applied noxious stimuli to various sites in nose and found the Sinus ostea as the most sensitive. Holmes[3] (1963) observed that the sinus headache is triggered by hyper sensitive nasal mucosa. Greenfield (1968) explained the mechanism of the referred pain. He stated that the afferents from nasal mucosa and cutaneous afferents pool in same sensory nucleus of 5th nerve which cause false localisation. Robert. M. Hansen[4] (1968) observed tha nasal headache & vaso motor headaches are indistinguishable. He also observed that the nasal headache can cause reflex stimulation of cervical plexus which can cause nuchal pain. He further observed that head pain was due to impaction of mucosa between hard structures of septum and lateral nasal wall and it resembles vasodilating type.

Wepsi & Stojan[5] (1970) observed that the causes of nasal headache are chronic mucosal irritation and direct contact between septum and mucosa of turbinates.

Schnosted & Madsen[6] (1986) observed that diagnostic cocainisation in head pain patients has not been tried in a scientific survey. Takeshima (1968) reported that sinusitis can be present with cluster headache.

Stammberger[7] and Wolf (1988) stated that headache can be of sinugenic origin even if not suspected in case history, which can be due to small lesion in ethmoid cells especially in key areas/ Negative findings on anterior & posterior rhinoscopy & conventional radiographs don't rule out a sinus causation. they further reported that combination of diagnostic endoscopy and CT provides the maximum information, two modalities being adjunctive.

They further postulated that the release of substance - P is responsible for rhinogenic head pain. They reported that the pressure exerted on nasal mucosa by polyps, mucosal swellings or other reasons can be enough to trigger SP - mediated pain sensation via afferent C fibres.

Our observations in present study are in conformity with above workers. We find that the small lesions in key areas, which are missed on anterior & posterior rhinoscopy & conventional radiographs, produce considerable head pain. These small changes which were seen only in CT or endoscopy included small anatomical variations of uncinate process, aggar nasi & ethmoidal bulla. The other changes included small mucosal & polypoidal changes in key areas and localised posterior septal deviations. The latter was a significant finding as this posterior deviation was not appreciated on anterior rhinoscopy. Concha bullosa was found to be one of the common causes of head pain. Minor Surgical Procedures like conchoplasty, infundibulotomy, Partial M. turbinectomy, M. Meatal Meatotomy & anterior ethmoid clearance gave excellent results in relieving head pain. Patients who had undergone septoplasty earlier were also relieved by such procedures.

Conclusion:

C.T. Scan and nasal endoscopy are of great help in the diagnosis and management of those headache patients who do not have either clear rhinogenic cause or clear medical cause of headache.

These two modalities should be routinely used in case of Sino-nasal disease.

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EXPERIENCE WITH MECKEL'S DIVERTICULUM

Rajiv Gupta M.S; Sheetal Singh M.S; B.S. Pathania M.S.

Abstract: *Twenty patients of Meckel's diverticulum encountered at laparotomy over a period of two years from December 1997 to November 1999 in Surgical emergency are analysed. The majority of the patients were asymptomatic and represented an incidental finding at laparotomy. The most common clinical presentation in symptomatic cases was intestinal obstruction (62.5%) due to fibrous band connecting the Meckel's diverticulum to the umbilicus. All the patients were subjected to operative therapy. Intestinal Resection of the segment bearing Meckel's diverticulum with end to end anastomoseis tomatic cases, while diverticulectomy was done in asymptomatic cases found incidently. There was no significant post-operative morbidity and there was 0 percent mortality.*

Key Words: *Meckel's diverticulum, congenital, Diverticulectomy.*

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Introduction:

Meckel's diverticulum is the most frequent congenital malformation of the Gastro-intestinal tract and occurs in about 2% of population. Incomplete obliteration of the vitello-intestinal duct forms the Meckel diverticulum that always occurs along the anti-mesenteric border of the illeum usually two feet proximal to ileocaecal junction and is approximately two inches long. In most cases Meckel's diverticulum is asymptomatic and is detected incidentally at post-mortem or laparotomy. Even in symptomatic cases, diagnosis can be made with certainty only at operation and pre-operative diagnosis of the condition is very rare. A surgeon may not see a single case of Meckel's diverticulum through-out his career, but we have encountered 20 cases of Meckel's diverticulum at laparotomy in a period of two years from December 1997 to November 1999 in surgical emergency, Government Medical College, Jammu and have analysed our experience with Meckel's diverticulum, which forms the basis of this study.

Material and Methods:

This study is based on 20 patients of Meckel's diverticulum encountered over a period of two years (Dec. 1997 to November 1999) in 50 emergency duties as a Registrer in the Post-graduate department of Surgery, Government Medical College, Jammu. Various para-meters including age, sex, presentation, pathology, Surgical complications, operative treatment and the associated morbidity and mortality were taken into consideration. The majority of the cases were found in second and third decades of life and were discovered incidently at laparatomy. All the patients were subjected to operative treatment and were put on post-operative I.V. fluids and Ryle's tub suction alongwith injectable antibiotics and the results of the study were analysed.

Results

Twenty patients of Meckel's diverticulum encountered over a period of two years (Dec. 1997 to Nov. 1999) have been analysed. Although, found at all ages, the majority of patients were found in second and third decades of life. Table shows the distribution of these cases according to the age and sex. The youngest patient in the study was two years in age and the eldest patient was 59 years in age. The male to female ratio was 1:5:1. Out of 20, 12 patients (60%) were asymptomatic and represented an incrdental finding at laparotomy and only 8 patients (40%) had pre-operative symptoms. The most common clinical presentation in symptomatic cases was intestinal obstruction (62.5%) due to fibrous band connecting the Meckel's diverticulum to the umbilious.

Table: Age and Sex Distribution

Age in Years	Male	Female	Total
0-20	2	2	4
11-20	4	3	7
21-30	3	2	5
31-40	1	1	2
41-50	1	0	1
51-60	1	0	1
	12	8	20

In our series, one patient (12.5%) presented with umbilical fistula and two patients (25%) had features of inflamation and were clinically diagnosed as Acute appendicitis. There was no case with haemorrhage (Malena), intussusception, Litre's hernia or tumor in our series.

Size and Site:

The size of Meckel's diverticulum varied from 2-10 cms and they were found to be located 40-60 cms proximal

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to ileo-cascal junction along the anti-mesenteric border of ileum.

All the patients were subjected to operative treatment. Intestinal Resection of the segment bearing Meckel's diverticulum with end to end anaestomosis was performed in symptomatic cases, Whole diverticulectomy was done in asymptomatic cases found incidentally. The specimens subjected to Histopathological examination revealed normal mucosa in 17 patients (85%) and heterotopic mucosa in 3 patients 915%). There was no significant post-operative mortality and there was 0 percent mortality. Only one case (5%) where resection and end to end anastomosis was done showed post-operative complication in the form of leak from anastomosis on 5th post-operative day. This patient was re-explored twice and recovered. Mean hospital stay was 8 days, except in one case of complication, it was 2½ months).

Discussion:

Meckel Diverticulum is the most common congenital malformation of the Gastro-intestinal tract and occurs in 2% of Population. Incomplete obliteration of the vitello-intestinal duct forms the Meckel diverticulum that always occurs along the anti-mesenteric border of illeum usually 2 feet proximal to illo-caecal junction and is approximately 2 inches long. Meckel diverticulum has all the 3 coats of intestinal wall and has got its own mesentery and an independent blood supply. About 20% cases show heterotropic mucosa, mostly gastric mucosa.

Various Forms of the Anomaly are as follows:

1. Whole of the vitello-intestinal duct remains patent and results in vitello-intestinal Fistula that communicates externally with umbilicus and internally with ileum.
2. Only half of the portion communicating with the illeum remains patent and the other end is blind, hanging freely. This is the most common variety of Meckel diverticulum.
3. Most of the portion of vitello-intestinal duct gets obliterated and forms a fibrous band connecting ileum with the Umbilicus.
4. Central portion of vitello-intestinal duct remains patent, while the proximal and distal portions get obliterated resulting into enterocystoma.

Symptomatology:

In most cases, Meckel diverticulum is asymptomic and is detected incidentally at Post-mortem or Laparotomy. Even in symptomatic cases, diagnosis can be made with certainty only at operation. Various symptoms can be as under:

1. Haemorrhage from peptic ulceration of a Meckel diverticulum.
2. Inflamation of Meckel diverticulum resulting into diverticulitis,and may lead to perforation of the diverticulum that can result either into a localised abscess or general peritonitis.
3. Intestinal obstruction from Band, Torsion, Intussusception or obstruction within a hernia.
4. Gangrene secondary to axial torsion.
5. Umbilical fistula due to patent vitello-intestinal duct.
6. Littre Hernia.
7. Neoplasm (Carcinoid)

Patients most likely to develop symptoms from Meckel Diverticulum are:-

1. Those under age of 40 years.
2. If patient is male.
3. When Meckel Diverticulum is 2 centimeters or more in length.
4. Presence of Hetrotopic Mucosa for which indirect evidence is the presence of Submucosal or mucosal nodularity, scarring or inflamation.

Pre-operative diagnosis of Meckel diverticulum is very rare, though ectopic gastric mucosa in a Meckel diverticulum is visualised by a technetiums scan of the abdomen using TC 99M per technetate.

Conclusion:

Keeping in view the complications a Meckel's diverticulum can produce and with no added morbidity and mortality after surgical intervention, we recommend that Meckel's diverticulum should be operated upon if found incidently or otherwise, though a wide-mouthed, thin-walled, unattached diverticulum in an elderly patient can be left as such. Resection and anastomosis is preferred over simple diverticulectomy when bowel adjacent to Meckel's diverticulum is oedematous or the site of peptic ulcer or when ileum is of small calibre so as to ensure complete excision of ectopic tissue.

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CLINICOEPIDEMIOLOGICAL PROFILE OF BIRTH ASPHYXIA IN KASHMIR VALLEY

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Abstract; *Birth Asphyxia (Inability of the baby to initiate and sustain spontaneous breathing immediately after birth) is very common in Kashmir Valley when compared with its incidence seen in other parts of the country. It has been attributed to the lack of the adequate antenatal care whereby high risk pregnancies are not picked and also there is significant deficiency of the experienced obstetric and neonatal staff and infrastructure which leads to the higher incidence of birth Asphyxia and the management failure of such patients.*

Key words: Birth Asphyxia, Apgar score, Resusciation

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Introduction:

Birth Asphyxia in its simplest form is defined as the inability of the newborn baby to initiate or sustain the spontaneous breathing immediately after birth. Or in other words if the baby has gasping or inadequate breathing or no breathing at 1 minute[10,12]. Another entity that is known as fetal hypoxia is an antenatal problem. The two (fetal hypoxia after 28 weeks of gestation and birth asphyxia) together are described as perinatal hypoxia which is diagnosed by the presence of following criteria.

1. Umbilical cord arterial blood PH of <7 with a base deficit of >10 meq./l
2. Neonatal Neurological features Suggestive of HIE (Sizures, coma, hypotonia)
3. Multi organ dysfunction (e.g. cardiovascular pulmonary, renal)
4. 5 mts. Apgar score of 3 or less.[1]

The definition of birth Asphyxia has undergone many modifications till 1953 when virginia apgar an anaesthesiologist devised the scoring system for the evaluation of the wellbeing of the newborn infants. This scoring system named as apgar scoring system of ten points has been accepted universally.[2]

Material & Methods:

The present study is based on the analysis of ten years (1991 to 2000) data collected from the Deptt. of Neonatology SKIMS and various major maternity centres of Srinagar city (Capital city of Kashmir) some relevant informative data has been collected from some peripheral hospitals.

Observations:

(The study conducted revealed the total number of admissions received in the Nursery of SKIMS during the past ten years (1991-2000) has been 5734, out of which the No. of birth Asphyxia cases was 1597 (27.85%). Total No. of live deliveries conducted in the catchment maternity units around the SKIMS over the same period was 18795 and the birht Asphyxia cases constitute 8.49% of these live births. The relevant statistical data is shown in Table-I.

The incidence of birth Asphyxia in Lalded Hospital, the biggest obstetric/maternity centre of the valley, is even higher where averagely fifty or more deliveries are conducted in every 24 hours, out of which 16 babies are referred to the Neonatology section of one or the hospital. Majority of referrals are for the respiratory problems and the commonest cause of respiratory problem is related to birth Asphyxia.

The mortality of severe birth Asphyxia has been detected as very high (44.48%) which is consistent with most of the other studies. Among the patients of mild birth Asphyxia only three patients died all of them had developed sepsis, the diagnosis of which was confirmed by positive blood cultures.

The commonest association of birth Asphyxia has been identified as -Prematurity which has a direct bearing on the incidence of birth Asphyxia, other risk factors association with birth Asphyxia are given in Table-II.

Hospital course of the patients varied according to the severity of the Asphyxia and the time interval that had actually passed between the occurance of Asphyxia and the admission in NICU. The presence of complications of the Asphyxia was very important determining factor in the morbidity and mortality of the patients.

Discussion:

The study conducted revealed the incidence of birth Asphyxia in Kashmir valley as very high when compared

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with what has been reported from other parts of the country and various developed countries around the world. The incidence of birth Asphyxia in the developed countries has been reported as 1.5 percent and in India it has been reported 5 to 10 percent in different studies conducted in different parts of the country[1,3,4,5]. While as in our present study considering the deliveries conducted in all the major maternity centres of Srinagar city the rate of birth Asphyxia has been aestimated as 8.9 per hundred live births which is a significantly higher incidence, the actual incidence is even higher because many cases of birth Asphyxia in the minor delivery centres (including home deliveries) remain unreported.

Table -I

Statistical data (of ten years period) showing parameter of birth asphyxia in skims and its associated maternity centres

	Number	Percentage	Mortality
Total live deliveries in the catchment hospital	18795		
Total Admissions in the Nursery	5734		
Total Birth Asphyxia patients admitted	1597	8.49% of total live births 27.85% of total Nursery admission	
Mild Birth Asphyxia	175	10.95% of total birth Asphyxia cases	3 (1.71% of mild birth Asphyxia cases)
Moderate birth Asphyxia	895	56.04% of total birth Asphyxia	62 (6.92% of moderate birth Asphyxia cases)
Severe Birth Asphyxia	526	32.93% of total birth Asphyxia	234 (44.48% of severe birth Asphyxia cases)

Total deaths = 299 (18.72% of total birth Asphyxia patients)

The higher incidence of birth Asphyxia in Kashmir Valley has been attributed to the lack of Health Education in the public and inadequacy of the required infrastructure (e.g. medical staff, properly trained adequate paramedical staff) there is lack of adequate antenatal care whereby high risk pregnancies remain unidentified, finally there is lack of the major and minor equipments required for the investigative and supportive measures in the intrapartum and neonatal care.

In the present study the major proportion of the birth Asphyxia cases is formed by moderate and severe birth Asphyxia patients, while as the incidence of the mild birth Asphyxia has been estimated to be only 10.95% (Table-I) of the total cases, which is far less than what has been reported from around the country and outside the country[6]. It deserves an explanation, that has been hypothesized on the basis that majority of the cases of mild birth Asphyxia are either ignored or treated locally by primitive and primary measures and thus remain unreported and this hypothesis further adds to the evidence in support of the fact of inadequacy of existing easily accessible basic medical facilities in the valley of Kashmir.

To avoid the occurance of the perinatal hypoxia and its complications the anatenatal surveillance of the pregnant mothers is a very important way to pick the high risk pregnancy cases and keep them under close monitoring especially after 28 weeks of pregnancy and ensure the safe delivery of a full term baby.

Further according to the score devised by Virgina: Apgar it is the score in first five minutes that bears the prognostic value for the future neuromotor outcome of the baby[9,11]. As such these first few minutes in the life of the new born are very critical and it is the responsibility of the obstetric and nursery staff to ensure the safe and smooth passage of the baby from the mothers womb to an independent life.[7,8]

Summary:

An overall incidence of birth Asphyxia of 8.49%, with moderate and severe constituting bigger proportions and mild birth Asphyxia unusually constituting a smaller proportion of it has been detected. The study itself indicates that the actual incidence of birth Asphyxia must be even higher as the actual number of mild birth Asphyxia cases remains unreported. Improvement in the health care facilities especially the antenatal ones is the only measure to prevent the occurence of Asphyxia in perinatal ones is the only measure to prevent the occurrence of Asphyxia in perinatal period and the improvement in the infrastructure of neonatal intensive care units goes the largest way in the management of the patients of birth Asphyxia.

Table-II: Antepartum factors

1. Maternal hypertension
2. Maternal Diabetes
3. Postmaturity
4. Fetal Malpresentation
5. Multiple gestations.
6. Rh. Iso immunization.
7. Bad obstetric history
8. Poly or oligohydramious
9. Maternal drug abuse
10. Congenital malformations

Intrapartum factors:

1. Premature labour
2. Fetal distress
3. Antepartum hemorrhage
4. Cord prolapse
5. Cord around the neck
6. Meconeum staining of liquour
7. Premature rupture of membranes
8. Prolonged labour

9. Use of Narcotics in mother
10. General Anaesthesia in mother

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"ROLE OF LIPIDS IN STROKE"

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ABSTRACT: *Present study was conducted to understand the role of lipids in stroke. 100 stroke patients which included 88 Ischemic and 12 haemorrhagic,were compared with equal number of age and sex matched healthy controls. VLDL-Cholesterol, total lipids were significantly raised whereas LDL-cholesterol and HDL-Cholesterol were significantly lower in cases than controls (p value 0.000 & 0.000 respectively). Total cholesterol and HDL-cholesterol were significantly lower in haemorrhagic stroke patients as compared to controls (p value 0.000 and 0.000 respectively). Total cholesterol and VLDl-cholesterol were significantly elevated in haemorrhagic than ischemic stroke patients (p value <.001 & <0.000 respectively). Thus we conclude that total lipids, LDL-cholesterol and VLDL-cholesterol are increased in all type of stroke patients and important risk factor for them. Low cholesterol level is important risk factor in haemorrhagic stroke patients and increased VLDL-cholesterol level significant risk factor in ischemic stroke patients.*

Key words: *Cholesterol, HDL-cholesterol, Haemorrhagic; Ischemic; LDL-Cholesterol; Lipids; Stroke; Triglycerides; VLDL-cholesterol.*

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INTRODUCTION

A stroke indicates the relative abrupt onset of non-convulsive focal neurological deficit resulting from disease of the arteries or veins that serve the central nervous system. It is the third leading cause of death in the world. The strokes are either ischemia-infarction or intracranial haemorrhages, the former comprising about 85-90% in the western world while haemorrhages constitute large percentage in Asia.[1] Many temporal patterns of stroke syndrome are recognized: Transient ischemic attack's (TIA's); reversible ischemic neurological deficits (RIND's), completed stroke, and stroke in evolution. TIA is a short-lived episode of neurological dysfunction caused by a reversible interference of blood supply to an area of retina or brain, followed by complete recovery within 24 hours of the episode.[(2)] RIND is the temporal profile of the stroke syndrome in which the focal neurological ischemic deficit lasts longer than 24 hours but resolves with complete recovery within 3 weeks.[3] 'Completed' stroke is the condition in which the deficit is prolonged and often permanent causing demonstrable parenchymatous changes.[(4)] Stroke in Evolution on the other hand describes the temporal profile in which the neurological deficit occurs in a stepwise or progressive fashion, culminating in a major deficit in the absence of treatment.[5]

Several risk factors are known to increase liability to the stroke. The most important of these are hypertension, heart isease, atrial fibrillation, diabetes mellitus, smoking of long duration, hyperlipidemia, oral contraceptives and systemic diseases with hypercoagulable state.[6]

The relationship between lipids and lipoproteins with ischemic cerebro-vascular diseases (ICVD) is not as clear as with coronary heart disease (CHD).[7] However, there are several clinical trials that have shown a decrease in stroke incidence with the use of drugs that lower the serum lipids.[6] The aim of the present study is to understand the role of lipids and lipoproteins in the etiology of stroke.

MATERIAL AND METHODS

One hundred stroke patients were taken up for study over a period of 10 months. They were compared with equal number of age and sex matched healthy controls. Stroke in the patients was confirmed by computed axial tomography of the brain. Lipid profile estimation was conducted within 48 hours of the ictus from 20ml of venous blood obtained from the patients. Controls were studied in the similar way. Patients with hepatic, renal, thyroid or any other neurological disorder, women consuming oral contraceptive pills or any other disorder affecting lipid metabolism were excluded from the study.

Total lipids were determined according to method of Zohier N et al.[(8)] A commercially available kit (Cat No. TL100) obtained from Randox UK was used. Analytical details followed were in accordance to the applicator sheet provided with the kit. Serum lipids react with H_2SO_4 and vanilin to form a pink coloured complex which was read

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at 540nm. A standard was treated in the same way as the sample.

Total cholesterol levels were obtained according to the method of Trinder.[9] P.A. commercial kit obtained from Boehringer Manheim, Germany was used. Analytical details were followed as per the applicator sheet provided with the kit. Hitachi 704 analyzer was used in the study.

Triglycerides were determined according to the method of Jacobs et al[10] which is based on the enzymatic hydrolysis of triglycerides with lipase and formation of chromogen from H_2O_2, 4-aminophenozone and 4-cholorophenol in presence of peroxidase. The commercial kit (Cat No. TR210) from Tandox UK was used for the assay on Hitachi 704 analyzer.

VLDL-cholesterol and LDL-cholesterol were calculated using Friedwald's formula.[11]

VLDL-cholesterol = Triglycerides/5

LDL-cholesterol = Total cholesterol-(HDL cholesterol + Triglycerides/5)

HDL cholesterol was determined by enzymatic method of Bernstein M, et al.[12]

TABLE I: SEX DISTRIBUTION OF STROKE PATIENTS AND CONTROLS

	Males	Females	Ratio
Patients	59	41	3:2
Controls	59	41	3:2

TABLE II: AGE DISTRIBUTION OF STROKE PATIENTS AND CONTROLS

Age in years	Patients	Controls
<40-49	6	4
50-59	60	56
>60	34	40

TABLE III: COMPARISON OF VARIOUS LIPID PARAMETERS BETWEEN CASES AND CONTROLS (BOTH HAEMORRHAGIC AND ISCHEMIC)

	Levels (n=100) Cases	(n=100) Controls			
Name of lipids	Mean±SD	Mean±SD	Range	t	P
Cholesterol	191.58 ±43.78	183.92 ±42.05	109-305	-.89	0.374
LDL-cholesterol	54.88 ±17.49	92.54 ±45.25	5-216	5.49	0.000
VLDL-cholesterol	100.98 ±46.15	3[illegible].84 ±19.59	13-98	-8.76	0.000
Total lipids	945.02 ±244.71	756.6 ±81.77	650-1950	-4.78	0.000
Triglycerides	185.26 ±86.87	177.08 ±81.77	67.993	-.48	0.629
HDL-cholesterol	36.96 ±17.22	52.46 ±11.99	22-86	5.22	0.000

TABLE IV: COMPARISON OF VARIOUS LIPID PARAMETERS BETWEEN ISCHEMIC STROKE PATIENTS V/S CONTROLS

	Levels (n=88) Cases	(n=100) Controls		
Lipid parameters	Mean±SD (Range)	Mean±SD (Range)	t	P
Cholesterol	199.07 ±40.78 (122-305)	183.92 ±42.05 (58-280)	-1.77	0.081
LDL-cholesterol	53.11 ±17.66 (36-216)	92.54 ±45.25 (6-185)	5.42	0.000
VLDL-cholesterol	110.36 ±40.23 (13-98)	38.84 ±19.59 (16-93)	11.16	0.000
Total lipids	947.75 ±257.80 (650-1950)	756.60 ±134.02 (400-963)	4.59	0.000
Triglycerides	188.05 ±90.09 (69-493)	177.08 ±81.77 (86-464)	-.62	0.538
HDL-cholesterol	37.50 ±17.84 (22-86)	52.46 ±11.99 28-68)	4.82	0.000

TABLE V: COMPARISON OF VARIOUS LIPID PARAMETERS BETWEEN HAEMORRHAGIC STROKE PATIENTS V/S CONTROLS

	Levels (n=12) Haemorrhagic Stroke Patients	(n=100) Controls		
Lipid parameters	Mean±SD (Range)	Mean±SD (Range)	t	P
Cholesterol	136.67 ±17.60 (109-154)	183.92 ±42.05 (58-280)	2.71	0.009
LDL-cholesterol	67.83 ±9.37 (5-64)	92.54 ±45.25 (6-185)	1.23	0.191
VLDL-cholesterol	32.17 ±22.46 (20-47)	38.84 ±19.59 (16-93)	00.78	0.440
Total lipids	925.00 ±121.45 (750-1050)	756.60 ±134.02 (400-963)	-2.93	0.005
Triglycerides	164.83 ±59.92 (102-236)	177.08 ±86.46 (86-464)	0.35	.7248
HDL-cholesterol	33.00 ±12.08 (54.80)	52.46 ±11.99 (28-68)	3.75	.000

RESULTS

One hundred patients and equal number of age and sex matched healthy controls were studied. Patients comprised of 59 males and 41 females (M:F 3:2) and controls comprising of 59 males and 41 females (M:F 3:2) (Table I). Maximum number of cases (60%) were observed in age group of 50-59 years. Same was observed in control group (Table II). Out of 100 cases, 88 had ischemic while

TABLE VI: COMPARISON OF VARIOUS LIPID PARAMETERS BETWEEN ISCHEMIC STROKE PATIENTS AND HAEMORRHAGIC STROKE PATIENTS.

	Levels			
Lipid parameters	(n=88) Ischemic Cases Mean±SD (Range)	(n=12) Haemorrhagic Contros. Mean±SD (Range)		P
Cholesterol	199.07 ±40-87	136.67 ±17.60	3.67	.001
LDL-cholesterol	53.11 ±17.66	67.83 ±9.37	-1.99	.0521
VLDL-cholesterol	110.36 ±40.23	32.17 ±22.36	4.64	.0000
Total lipids	947.75 ±257.80	925.00 ±121.45	.21	.833
Triglycerides	188.05 ±90.09	164.83 ±59.92	.61	.545
HDL-cholesterol	37.50 ±17.84	33.00 ±12.08	.60	.554

12 had haemorrhagic stroke. Out of later group, 4 had sub-arrchnoid haemorrhage, while 8 patients had intra-cerebral haemorrhage.

VLDL-cholesterol, total lipids were significantly raised in cases than controls (p value 0.000), whereas LDL-cholesterol and HDL-cholesterol were significantly lower in cases than controls (p value 0.000) (Table III). Similar results were observed while comparing ischemic stroke patients and controls (p value 0.000) (Table IV). While comparing haemorrhagic stroke patients with controls, cholesterol and HDL-cholesterol were significantly lower in cases than controls (p value 0.000 & 0.000 respectively) (Table V). In comparing various parameters between ischemic stroke and haemorrhagic stroke patients, only cholesterol and VLDL-cholesterol were significantly elevated in former group (p<.001 & <0.000 respectively) (Table VI).

DISCUSSION

Stroke is one of the leading causes of mortality and morbidity among persons older than 60 years living in developing countries. Three main risk factors that have been found responsible for the stroke are: the elevated blood pressure, smoking and raised serum cholesterol. These risk factors are amenable to modification by diet, drugs or other interventions.[13] The present study was conducted to study the relationship between serum lipids and stroke of various types.

The study comprised of 59 males and 41 females. The age of the study population ranged from 36 to 87 years with maximum prevalence in the age group of 50-59 years with male preponderance (Table I & II). This is in contrast to various studies that revealed maximum incidence above 85 years age group. Although male predominance was observed in various other studies which was in accordance to our study.

After assessment of the lipid profile, the study revealed that VLDL-cholesterol and total lipids were significantly higher in all cases than their respective controls (p<.005) whereas no significant rise in the levels of cholesterol and triglycerides were observed in cases than controls (p values 0.374 and 0.629 respectively). HDL-cholesterol levels were significantly lower in the study cases (p<0.005) than their respective controls (Table III). Till date, no definite relationship has been established between lipids, lipoproteins and occurrence of stroke as it is seen with the coronary heart disease.[7] Cholesterol levels below 160mg% were associated with higher incidence of haemorrhage, higher levels of cholesterol were associated with large vessel atherosclerosis.[14,15] Kannel et al(1965)[16] found low cholesterol levels at the time of stroke as compared to the pre-stroke level. This was observed in the age group of more than 50-55 years which is in accordance to our study. Although Wolf 1983[17] and Rhodes 1984[18] did not notice any association of lipids with stroke. Taggart 1979[19] and Salonen 1983 showed definite relationship of lipids with stroke which were in contrast to our study. Framingham study showed an increased incidence of stroke in women with low levels of LDL-cholesterol.[6] These observations cannot be explained but suggested other factors such as levels of HDL-cholesterol that may be involved in accelerated atherosclerosis.[17]

Similar results were observed while comparing various lipid parameters between ischemic stroke patients and controls (Table IV). Dose dependent relationship between serum cholesterol and cerebral infarction has been observed.[21,22]

While Reed et al, (1986)[23] did not find any co-relation as was true with the present study, Sarti et al observed that high serum cholesterol levels are a risk factor for ischemic stroke[24] which is in contrast to our observations. Similar recent trials with statin drugs such as 4S, CARE, LIPID and WOSCOP have shown a decreased risk of stroke in the statin treated patients.[25] Yatsue & Loch, (1982)[26] and Tilvis et al, (1987)[27] observed higher triglyceride levels in middle aged men with brain infarction. They also observed a significant reduction in HDL-cholesterol levels in the ischemic stroke patients of age above 55 years. Both these observations were in contrast to the present study. In another study, higher levels of HDL-cholesterol were associated with a significant decrease in the risk of non-fatal stroke.[28]

While comparing haemorrhagic stroke patients with controls, cholesterol was found to be significantly low (136.6±17.60 V/S 182.90±42.05; p<0.005). HDL-cholesterol levels too were significantly lower in patients than controls (p<0.000). LDL-cholesterol, VLDL-cholesterol were also low but not statistically signifi-

Total lipids were significantly higher in patients than controls ($p<.005$) (Table V).

An inverse relationship of serum cholesterol and haemorrhagic stroke was observed in the present study. Similar findings were observed by Kagan et al, (1985) Yano et al, (1989) and Reed, (1990).[29,14,30]

Chopra and Prabhaker in 1979 observed increase in serum cholesterol, LDL-cholesterol and triglycerides in male and female stroke patients.[31]

In comparing various parameters between ischemic stroke patients and haemorrhagic stroke patients, only cholesterol and VLDL-cholesterol were significantly elevated in the former group of patients ($p<0.001$ & 0.000 respectively) (Table VI).

According to Jacob and Iso (1991), the ideal time for measurement of the serum lipid levels should be at the time of onset of stroke because malnutrition, liver and renal dysfunction may attribute for the same in next 3 months.[32] There is an additional advantage of including both fatal and non-fatal cases which were followed in the present study as well.

Thus we conclude that total lipids, LDL-cholesterol, VLDL-cholesterol are significantly increased and HDL-cholesterol decreased in all types of stroke patients and are important risk factors for them. Low serum cholesterol is an important risk factor in haemorrhagic stroke patients and increased VLDL-cholesterol is a significant risk factor in ischemic stroke patients.

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METASTATIC INTRAMUSCULAR MALIGNANT MELANOMA

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ABSTRACT: *A case is reported in which metastatic malignant melanoma had extensively infiltrated in the gluteal and pelvic muscles. It presented as low back pain and sciatica with a very tender area in the right gluteal region. The patient had a complete excision of nodular malignant melanoma from the back of right shoulder two years ago.*

The patient had received radiotherapy followed by a course of chemotherapy. Metastasis of malignant melanoma to skeletal muscle distant from the primary tumour is relatively rare and is scarcely reported in the English literature.

Key words. *Metastatic, intramuscular, melanoma*

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CASE REPORT

A 46-year-old caucasian man was referred by his general practitioner to our Accident and Emergency department with 6 weeks history of increasingly severe pain in the right sacro-iliac joint and buttock regions radiating to right thigh and leg. The pain was of insidious onset and the patient related it with a history of fall while playing with children 6 weeks ago. Coughing and weight bearing exacerbated the pain. This was accompanied with intermittent paraesthesia to right toes. There was some difficulty in passing urine and he had not opened his bowels for the last three days.

Examination of his back revealed loss of lumbar lordosis and slight tenderness at L4, 5 spine areas. There was an area of severe tenderness extending from the right sacro-iliac joint to the postero-lateral aspect of his right buttock. SLR was 30 degrees on right side and 60 on left. Ankle and knee reflexes were normal on both sides and toes were down going. Sensory and motor examination of lower limbs was unremarkable and distal pulses at ankle were palpable. The patient was apyrexial.

The patient had past medical history of nodular malignant melanoma at the back of his right shoulder two years ago. The lesion was completely excised and biopsy confirmed it to be nodular malignant melanoma – Breslow thickenss1.2mm and Clark's level 4. A month later patient underwent wide local excision of the area. The histology of the scar did not reveal any evidence of residual malignant melanoma. The patient was discharged.

A working diagnosis of right-sided L5-S1 disc prolapse was made and patient was admitted to the hospital for bed rest, analgesia and investigations.

Haematological investigations revealed Haemoglobin 15.2 gm/dl, WBC 16.8, platelets 317 and Plasma viscosity 2.34. The C-reactive protein was 34 and RA factor was negative. The LFT and U&E were within normal limits.

X-rays of lumbo-sacral spine were reported normal and chest x-ray did not reveal any evidence of bony or pulmonary metastatic disease.

Ultrasound examination of the region revealed a poorly defined hypoechoic mass measuring 4.5-cm in maximum dimension. Liver ultrasound showed multiple small hypoechoic metastasis in both lobes.

Bone scan demonstrated multiple skeletal metastasis, which were particularly visible in the ribs bilaterally.

MRI of pelvis (figure 1 and 2) revealed extensive involvement of gluteus medius and minimus. The mass was eroding the iliac bone medially and extending towards the sacro-iliac joint with extensive bony infiltration in both the iliac wing and right side of sacrum. There was a further mass present extensively with the right iliacus and early changes were developing within the psoas muscle. The left-sided bony pelvis and pubic symphysis were extensively infiltrated.

The patient was referred to the local oncology department where a course of local radiation to the painful area in the buttock was given followed by a course of chemotherapy.

DISCUSSION

Nodular malignant melanoma accounts for 20-25% of cutaneous melanoma in white individuals. It has tendency for early invasion of the dermis and have the capacity to metastasise widely to almost any organ or tissue in the body.

Direct muscle invasion by carcinoma is well recognised,

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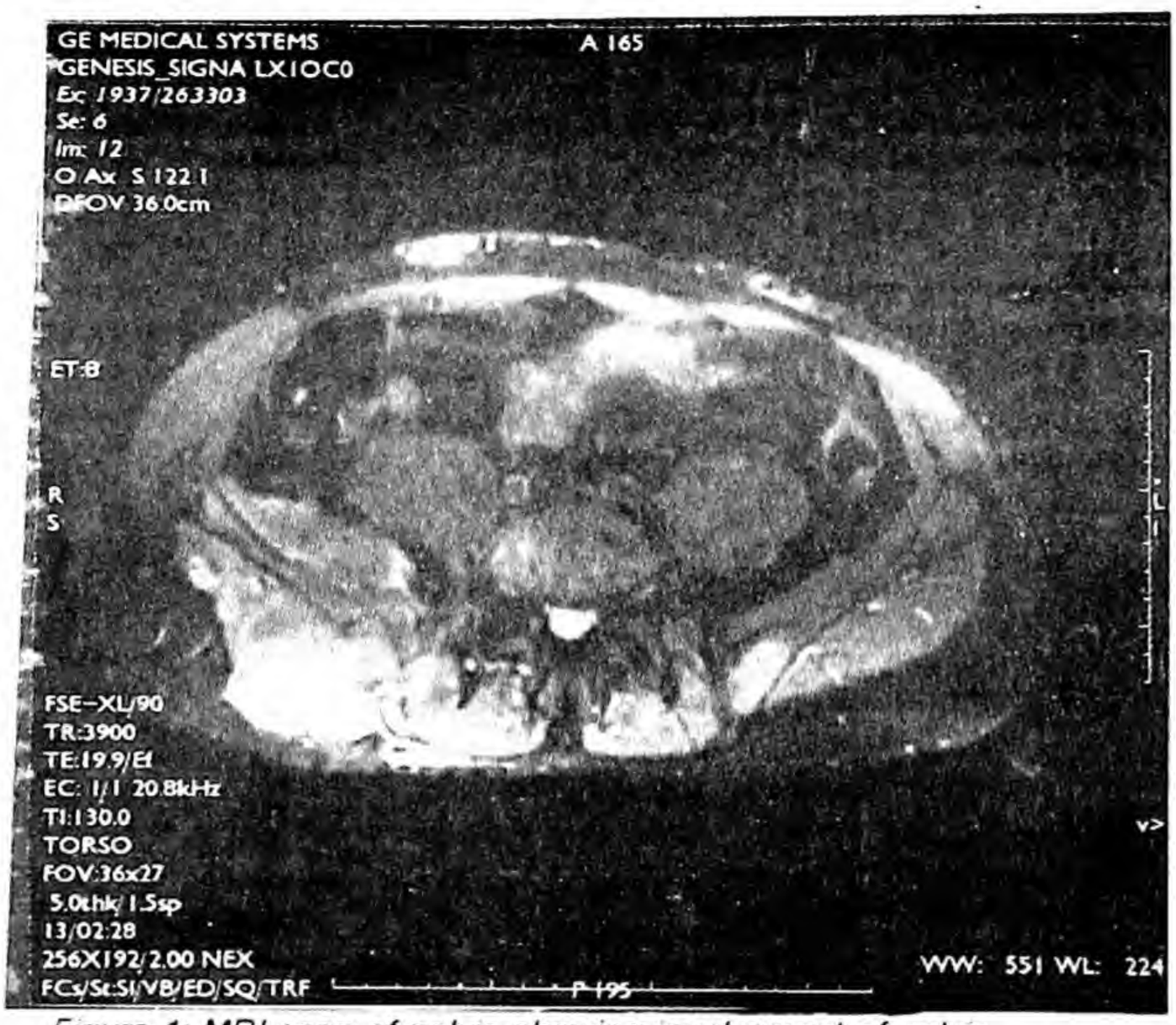

Figure 1: MRI scan of pelvis showing involvement of pelvic muscles

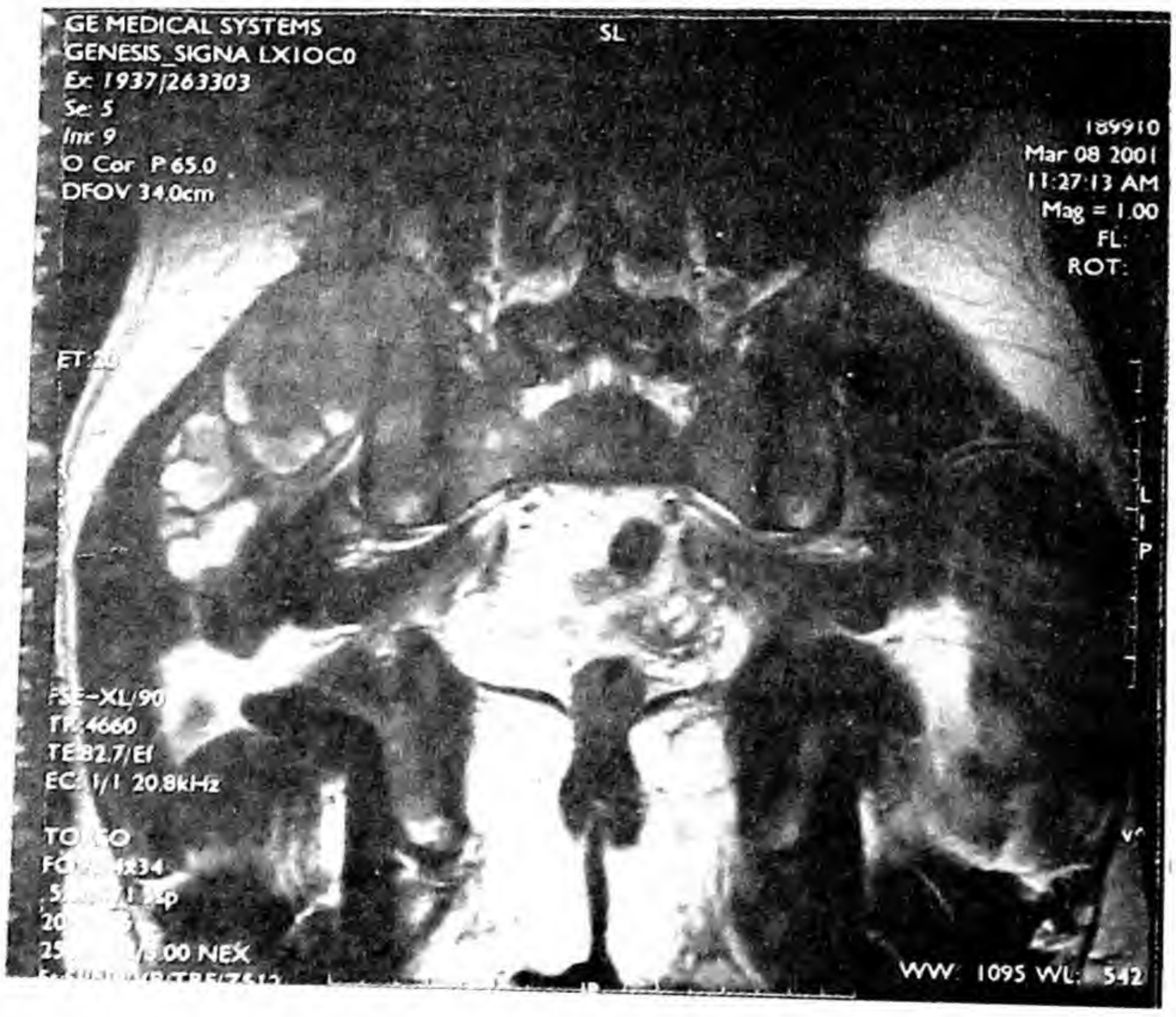

Figure 2: MRI scan of pelvis showing involvement of gluteal muscles

distant metastasis to skeletal muscle is uncommon[1]. Case reports of macroscopic metastatic malignant melanoma to skeletal muscle are rare.

More than one million new carcinomas are diagnosed each year nation-wide in USA. From 1979 through 1998 more than 54,000 new carcinomas were seen by Herring et al[1]. In contrast to the large number of new cases with cancer, the authors observed only 15 patients with metastasis to muscle during a 16 year period with only 2 patients with metastasis from melanoma, both in lower limb, in one involving Vastus lateralis and Gracilis in other patient. It is evident from the current series and review of the sparse amount literature, in which 52 cases were identified, that the clinical evidence of metastatic malignant melanoma to muscle is a rare event. Moss and Rees reported a case of metastatic malignant melanoma in sartorius muscle which appeared to be direct spread from the involved lymph node[2]. Autopsy series report a higher incidence of metastatic carcinoma to skeletal muscle and of these only two cases were found to be of malignant melanoma origin[3].

Herring et al suggested that the metastatic spread of carcinoma to muscle is a late event in the disease process with poor prognosis. However in this case an earlier metastasis of the disease had occurred which remained asymptomatic until widespread in the muscle. We suggest a need of regular follow up of these cases with a high index of suspicion even after complete surgical excision of the primary. MRI of any symptomatic area should be included as a part of the routine investigation.

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RECURRENT SOLITARY MYOFIBROMA IN AN ADOLESCENT BOY: A CASE REPORT AND REVIEW OF THE LITERATURE.

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Abstract: *A case of solitary myofibroma in an adolescent boy of 14 years of age is reported. The rarely reported cases of adult solitary myofibroma have so far not been associated with any bony or muscular involvement or recurrences. This case is reported to stress the importance of an entity like solitary myofibroma occurring at a relatively late childhood with unusual involvement of whole of the brachialis muscle and frequent recurrences.*

Key words: ***Myofibroma*** *– Adult- Myofibromatosis-soft tissue*

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Introduction

Solitary myofibroma is a benign neoplasm of soft tissues, which represents the adult counterpart of infantile myofibromatosis. Rare cases of superficial myofibromatosis in adults have been reported by Diamaru et al[1] and Smith et al[2]. Similar superficial lesions have been mentioned very briefly by Chung and Enzinger[3] while describing infantile myofibromatosis in 1981.

The myofibromas of infantile myofibromatosis usually present as a solitary or multiple nodules within first decade of life[3,4], usually before the age of 2 years. The lesions can be cutaneous or involve deeper structures such as muscles, bone and even visceral organs; the later at times, may lead to fatal outcome. In contrast myofibroma of adulthood type have been reported as solitary, superficial lesions with an entirely benign behaviour and unusual recurrence[5]. In sharp contrast to usual behaviour, we report a case of recurrent solitary myofibroma in an adolescent boy of 14 years at an unusual site with involvement of muscle, like in infantile myofibromatosis. To our knowledge, no adult cases have been reported with involvement of muscle, bone or visceral organ[5,6]. The purpose of this paper is to increase the awareness of this condition in adults at unusual locations with a potential for local recurrence.

Case Report

A 14-year-old boy reported to our hospital with painless swelling of right lower arm. He was operated twice during last two years with biopsy reported as nodular fascitis. The present swelling was there for last 8 months which was well circumscribed, firm extending from just above the cubital fossa to mid arm. The swelling was adherent to underlying bone and would become more prominent and fixed on resisted flexion of elbow. The overlying old scars and skin was free. There was no regional lymphadenopathy.

X-ray demonstrated a soft tissue swelling anteriorly over lower arm with scalloping of the underlying bone. There was also diffuse soft tissue ossification of the swelling (Fig.1).

Chest radiography, blood chemistry profile, urinalysis and complete blood count yielded normal results.

Operative findings revealed a soft tissue mass just under the skin involving almost whole of the muscle bulk of brachialis. It was about 8 cms. long globular, and fixed to underlying periosteum. Total excision of the mass along with brachialis muscle from origin to insertion with underlying periosteum was done (Fig 2). The overlying scarred skin was also excised.

The cut section of the tumour revealed a yellowish grey mass and microscopic section revealed typical features of myofibroma. Low power examination showed spindle cells with hypocellular areas merging with more densely cellular zones imparting a biphasic growth pattern although not as well marked as in infantile myofibromatosis. These cells were arranged in fascicles and whorls, of varying size. The cells especially the central areas had vesicular nuclei with light eosinophilic cytoplasm (Fig 3). There was mild to moderate pleomorphism. No mitotic figures were present. In more dense cellular areas, the stroma had rich vasculature with a haemangiopericytoma like growth pattern. There was no necrosis or intravascular tumorous growth.

After 4 months of follow up, a small nodule appeared under the skin at operation site, which was excised under local anaesthesia, and its biopsy again was reported as benign myofibroma. Possibly some portion of the tissue

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was left behind at the time of previous surgery. After 3 years of follow up, there is no evidence of recurrence of the lesion.

Discussion

Infantile myofibromatosis is a benign fibrous tumour reported primarily in infancy and children, with almost 90% of cases occurring before 2 years of age[6]. Superficial tumours, whether single or multiple are slow growing and have tendency to regress. Therefore, an incision biopsy to establish the diagnosis is adequate in most cases. Although Chung and Enzinger (1981)[3]

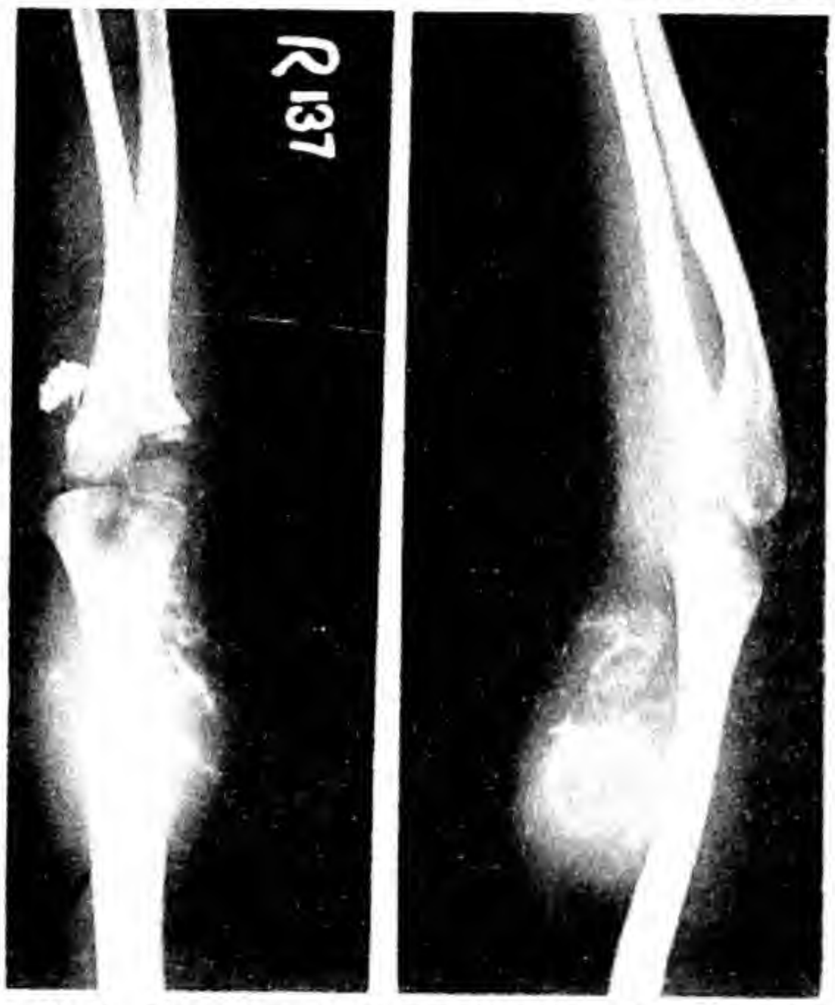

Fig 1. X-ray lower arm with elbow showing soft tissue swelling anteriorly with diffuse calcification and ossification of the tumour and scalloping ofthe underlying bone.

had seen two cases of solitary lesions in older patients, formal recognition of this variant was delayed until 1989 when Daimaru et al[1] and Smith et al[2] described their two series. There are only few other reported cases in the literature[5]. Reported adult cases were all superficial lesions, localized either in dermis or subcutaneous tissue, and solitary. This contrasts with infantile myofibromatosis in which involvement of deeper structures, such as skeletal

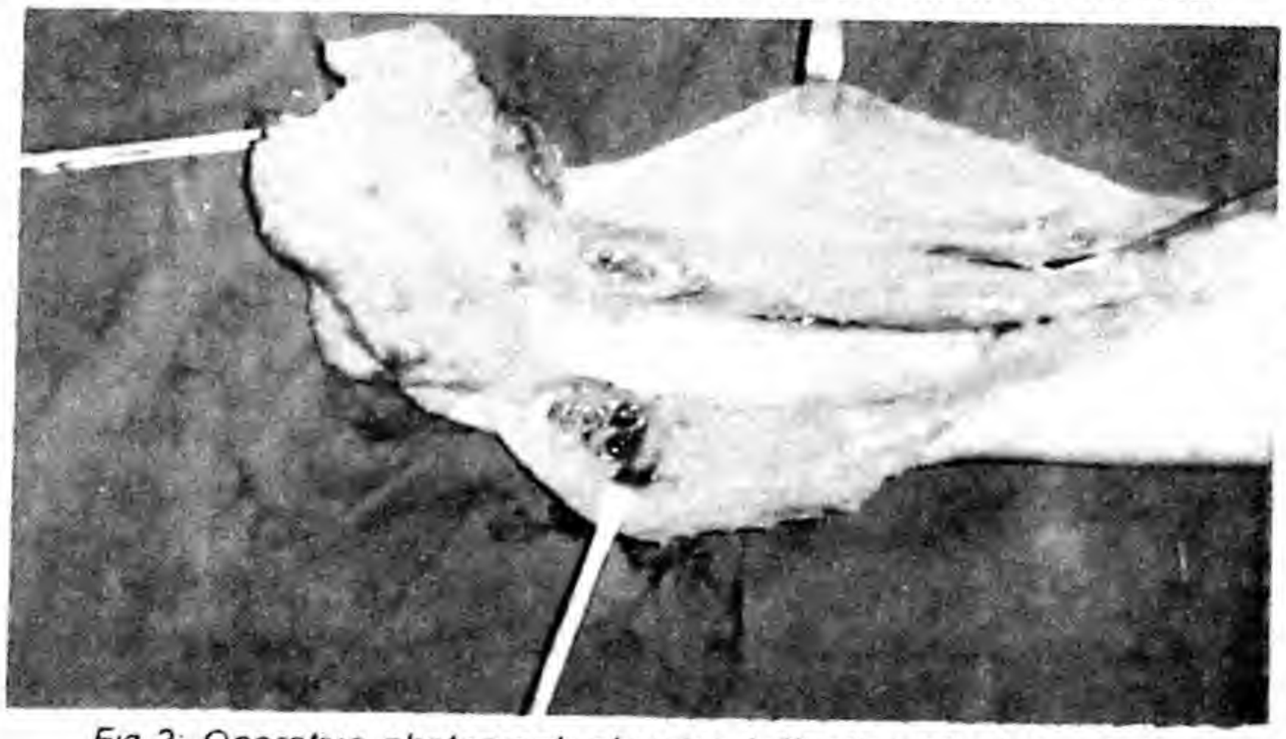

Fig 2: Operative photograph showing infiltration of whole of the brachialis muscle

Fig 3: Microphotograph shows whorls and fascicles of myofibroblasts with vesicular Nucleus and light eosinophilic cytoplasm.

muscle, aponeurosis, bone and even viscera, is seen in 50% or more of the cases[3]. Although occasional infantile cases have been noted to have an inherited basis[7], no such tendency is evident (as yet) in adult lesions reported.

In infantile myofibromatosis, the accurate diagnosis is important for two reasons. Firstly, recognition of this entity means that multicentricity (with visceral or bone involvement) will come as no surprise and will not be misconstrued as metastasis, as has happened in past. Secondly, not infrequent presence of necrosis, coupled with mitotic activity, and the occasional finding of vascular invasion[3], could easily lead to mistaken diagnosis of malignancy with all that this implies. Since spontaneous regression of these lesions is not uncommon[3], inappropriately aggressive treatment is particularly to be avoided.

The present case of solitary adolescent myofibroma was distinct regarding its infiltrative pattern-involving whole of brachialis muscle with secondary effects on underlying bone and recurrent behaviour. Differential diagnosis includes nodular fascitis, neurofibroma, benign histiocytoma, leiomyoma and leiomyosarcoma, dermatomyofibroma and haemangiopericytoma. Nodular fascitis is generally located in the subcutis and muscle as a circumscribed nodule or mass attached to superficial fascia. There is generally prominent myxoid background as well as scattered chronic inflammatory cells and occasional erythrocytes. Haemangiopericytoma pattern or zonation is not a feature of nodular fascitis. Leiomyosarcoma may demonstrate similar appearing cells in bundles and fascicles but it lacks characteristic haemangiopericytoma like vascular pattern and zonation. Leiomyosarcomas are generally more mitotic and more pleomorphic. In addition calcification, which is common in necrotic examples of myofibromatosis,[3] is not a feature of leiomyosarcoma. Infantile haemangiopericytoma is readily distinguishable by

its lack of an eosinophilic spindle cell component or calcification and by the fact that the vascular pattern would be even more prominent and the small tumour cells usually have almost no discernible cytoplasm. Furthermore, endothelial proliferation within the vascular channel is a common feature of the infantile form of haemangiopericytoma. Most fibrous histiocytoma show at least focal lipidization, giant cells, and storiform architecture. Dermatomyofibroma is ill-defined plaque-like dermal proliferation of fibroblasts and myofibroblasts, arranged parallel to the epidermis and does not show the biphasic pattern of a solitary myofibroma.

In conclusion, the aim of presenting this case is to stress the importance of an entity like myofibroma and its occurrence at a relatively late childhood, unusual location and potential for multiple recurrences.

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RHABDOMYOSARCOMA OF AN ADULT FOOT WITH AN EXPANSIVE GROWTH BETWEEN THE METATARSALS: A CASE REPORT AND REVIEW OF THE LITERATURE

Naseer Ahmed Mir; Javeed Ahmed Bhat; Abdul Rasheed Rather

Abstract: A case of rhabdomyosarcoma of foot is reported in an elderly woman. The importance of early diagnosis and treatment is suggested to improve chances of survival of this high-grade tumour. Also it is stressed that bowing of the metatarsal could also occur with these high-grade infiltrative tumours and this radiological finding should not always be viewed as due to a benign slow growing tumour.

Key words: Soft tissue tumour-Rhabdomyosarcoma-Bowing-Saucerization-Foot radiology.

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Introduction

The soft tissue sarcomas of the foot are rare[1]. Rhabdomyosarcoma is the malignant tumour of striated muscle. It varies considerably in frequency and type among different age groups. Microscopically it can be sub divided into 3 main types: embryonal, alveolar and pleomorphic. Some tumours of course have mixed features. The embryonic and alveolar types occur in childhood and adolescents and are among the more common malignant tumours of these age groups. The classical pleomorphic type occurs in adults and is rare. Furthermore, the origin of the tumour from the small muscles is extremely rare in adults[2]. The bowing of tubular bones due to juxta cortical tumours is a finding suggestive of slow, expanding growth unlike the present case which demonstrated infiltrating pleomorphic rhabdomyosarcoma in spite of this benign radiographic feature.

Case Report

A 50-year-old obese woman reported with 6 months history of painless swelling of right foot between 1st and 2nd metatarsals. Examination showed a hard, non-tender swelling between metatarsals projecting mostly on dorsal aspect. X-ray revealed a soft tissue swelling between 1st and 2nd metatarsals with sclerosis and bowing of 2nd metatarsal (Fig 1). CT scan demonstrated a soft tissue swelling between 1st and 2nd metatarsals extending from planter to dorsal aspect without any surrounding well defined margins, more likely representing a tumour of an infiltrative nature (Fig 2). FNAC showed features of rhabdomyosarcoma but excision biopsy was advised for further confirmation. X-ray chest was normal.

Operative findings: A hard mass was found between 1st and 2nd metatarsal projecting planter as well as towards dorsal aspect and had to be approached on both sides. It was possibly arising from dorsal interossei and engulfing the surrounding tissues and projecting between the metatarsals more towards the dorsal aspect. The periosteum of the 2nd metatarsal was adherent to the mass and the mass was also surrounding the 1st metatarsal all around except medially. Excision biopsy was done which confirmed the diagnosis of pleomorphic rhabdomyosarcoma (Fig 3). A below knee amputation was subsequently performed keeping in view the gross infiltration and nature of the growth. Subsequent chemotherapy and localized radiotherapy was given. After 2 months of follow up, the patient started with hemoptysis due to extensive lung metastasis and expired.

Discussion

Rhabdomyosarcoma may arise anywhere in the body, but the head and neck region, genitourinary tract in the retroperitoneum and upper and lower extremities are the most common locations[3]. The pleomorphic type of rhabdomyosarcoma usually occurs in the extremities and is much less common than other two types. It has mostly been reported from proximal thigh. Its origin from some of the smaller muscles may not be obvious[2].

Radiological features are usually nonspecific. Infiltrative growth is a common finding, as seen in other high-grade malignant neoplasms[4]. CT scan or better MRI imaging is the most useful means of demonstrating the extent of the leison[3]. The deformity of the shaft of the long bone due to neoplasm is typically seen in slow growing expansive masses, presumably due to extrinsic pressure and remodeling. If the remodeling involves shaft of the tubular bone circumferentially, bowing may occur, and if the remodeling is limited to one side of the cortex,"saucerization"

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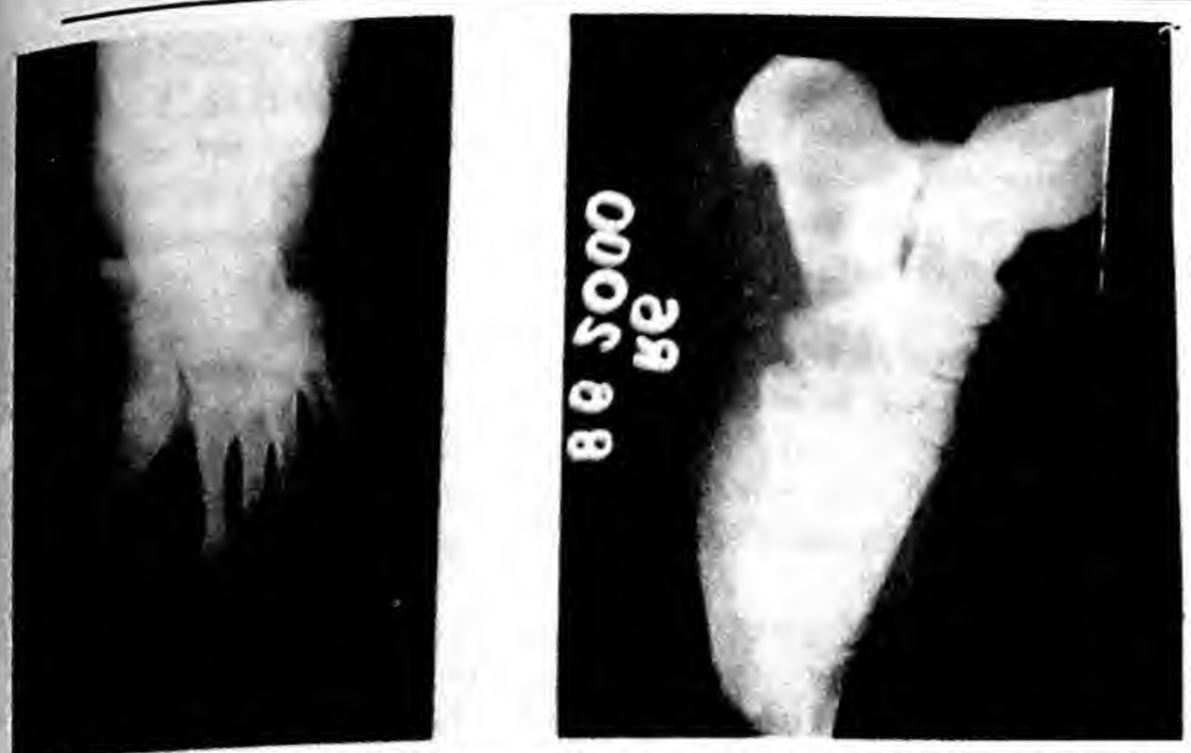

Fig. 1: X-ray right foot demonstrating a soft tissue swelling between 1st and 2nd metatarsals with sclerosis and bowing of 2nd metatarsal.

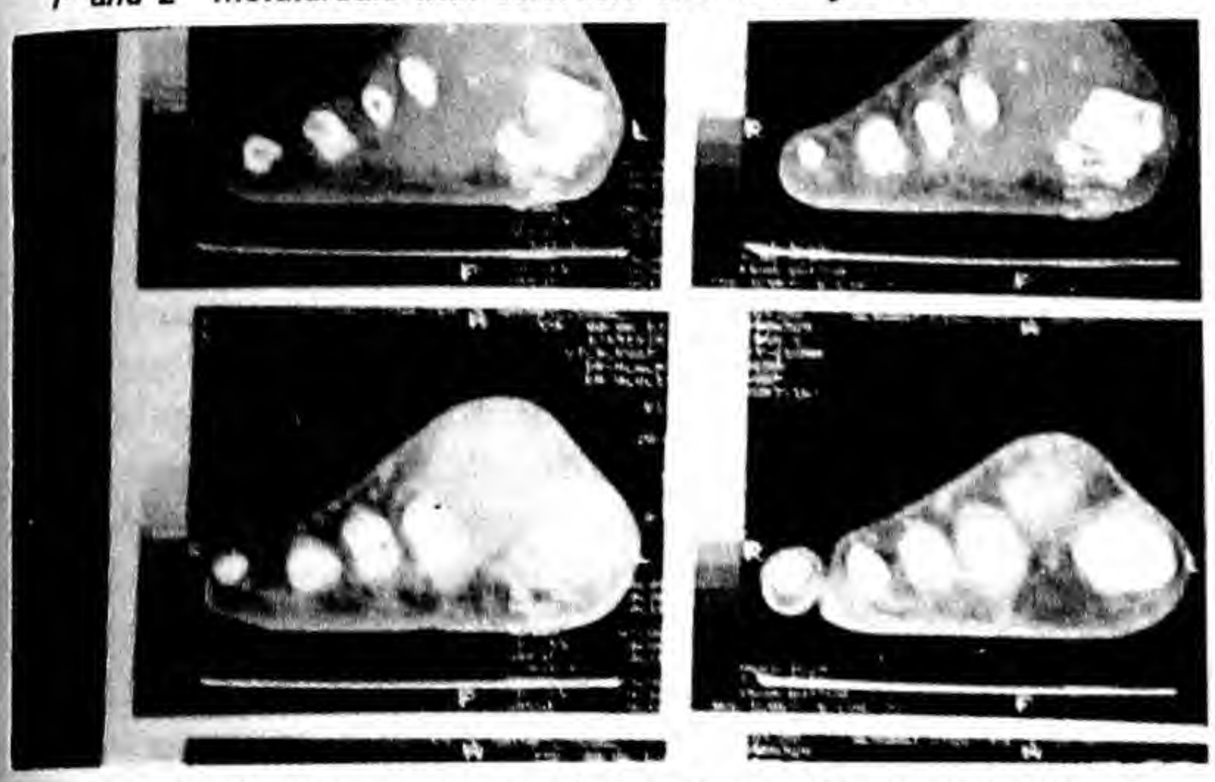

Fig. 2: CT Scan showing soft tissues swelling between the metatarsals extending from planter to dorsal aspect with ill-defined margins.

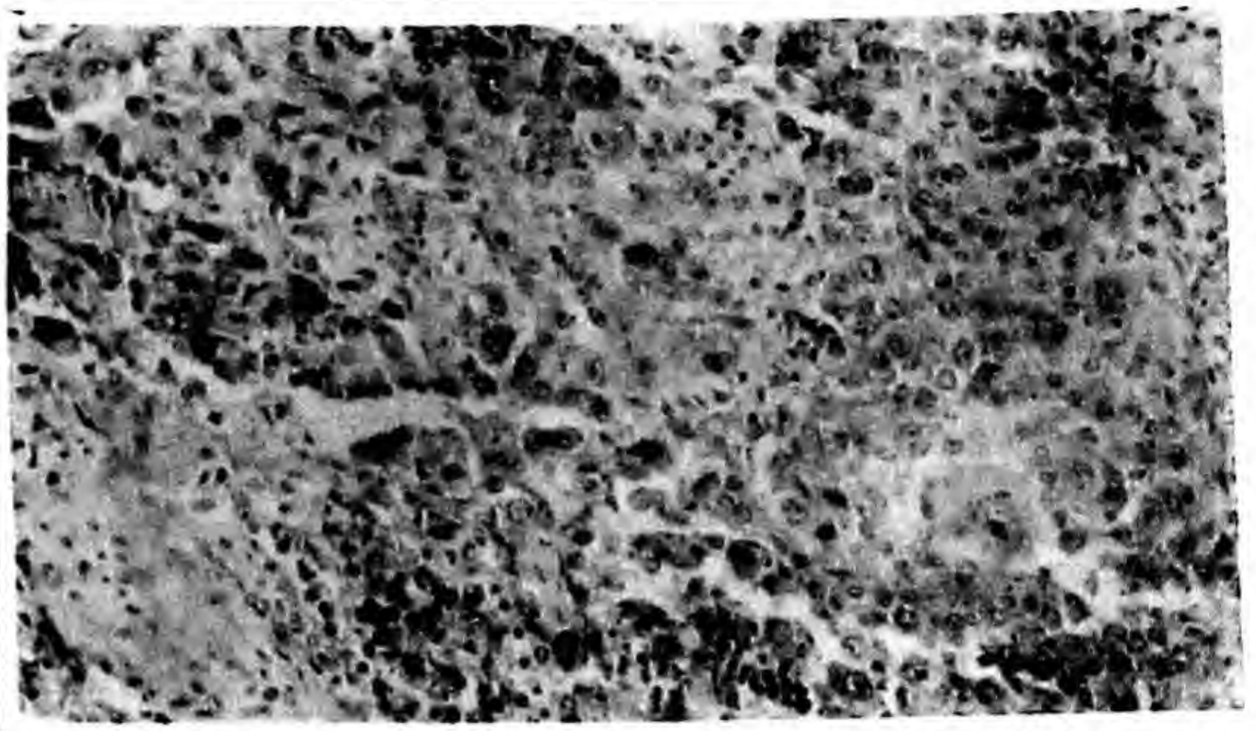

Fig. 3: Photomicrograph showing Rhabdomyosarcoma with tumour cells showing hyperchromatic pleomorphic nuclei with cytoplasm showing differentiation towards muscle (Rhabdomyoblasts). (H & E x 40).

may result. Saucerization is reported to be caused by an infiltrative process including Ewing's sarcoma, Fibrosarcoma, and Rhabdomyosarcoma of bone and soft tissue. Bowing of the shaft of long bones in high-grade lesions, although not well described previously, may be observed. It may be due to extrinsic pressure, infiltration, and remodeling[3].

In general soft tissue sarcomas of the foot are rare and treatment modalities remain unclear. Reese et al (1993)[5] reporting a case of rhabdomyosarcoma of foot, has found that prognosis was directly related to the extent of the disease. Delaying treatment or improper treatment could easily make difference between life and death. When a highly aggressive rhabdomyosarcoma is encountered, a planned formal excision with adequate margins is mandatory to achieve optimal results. Extremity rhabdomyosarcoma have relatively worse prognosis, which has been attributed to a higher frequency of alveolar histology, predilection to lymph node metastasis, and the presence of [illegible]

disease at diagnosis[6]. The proximity of neurovascular bundles and the sparsity of soft tissue coverage around the foot and ankle make adequate surgical treatment of these malignant tumours incompatible with a preservation of a functional foot. The most functional reconstruction and the way a preferred surgical margin may be obtained are through amputation. With foot and ankle sarcomas the ability to obtain local control has always been good, even if it requires amputation. Unfortunately the risk of distant metastasis remains significant. Most of the soft tissue sarcomas spread haematogenously and oftenly to the lungs. The role of chemotherapy in the suppression or prevention of metastasis and its effect on long-term survival continues to be evaluated[7]. Treatment approaches have changed substantially over the two decades during which these patients were treated. Radical surgery, once considered the treatment of choice, has been replaced by limb sparing surgery with radiation therapy added for local control[8]. In general it seems that major problem in treating soft tissue sarcoma is not local control but distant failure. Thus treatment recommended is combination of wide resection when possible- but marginal or even intra-lesion resections are acceptable with associated radiotherapy and prolonged systemic polychemotherapy[2]. In patients with favorable staging of the tumour (localized disease, completely resected and no evidence of regional lymph node involvement) over 80% survive for a long time[2].

The poor prognosis in our case was because of delayed presentation and treatment when possibly she had already micrometastasis in the lungs.

In conclusion, early diagnosis before distant metastasis improves chances of survival. Radiological features may be misleading in rhabdomyosarcoma of forefoot which may demonstrate [illegible] of metatarsal due to soft tissue tumour

thereby suggesting a slow growing expanding growth, leading to impression of benign nature of the lesion while as CT or preferably MRI imaging predicts more aggressive nature of the lesion.

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RHINOCEREBRAL MUCORMYCOSIS IN DIABETIC KETOACIDOSIS : A CASE REPORT.

Rubina Lone *MBBS*, Asifa Nazir *MBBS*, Tehmeena Wani *M.D*, D.K.Kakroo *M.D*

ABSTRACT: *Mucormycosis is a grave fungal infection with a very high mortality rate. It is a rare but serious fungal infection that rapidly attacks and usually kills its untreated victims, who are often acidotic, 'immunocompromised', or receiving desferrioxamine. Many reported cases have been poorly controlled diabetics. Synonyms are 'zygomycosis' or 'phycomycosis'.*

In this case, a young woman developed the complication following an episode of ketoacidosis, with the paranasal sinus being the most probable portal of entry . She was administered amphotericin B but died on the third day of admission.

KEY WORDS: *Mucormycosis. Diabetic ketoacidosis. Amphotericin B.*

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INTRODUCTION

Invasive mucormycosis is a rare but lethal opportunistic infection caused by ubiquitous fungi found in soil, bread, dust and spoiled foods.[1] The causative organisms may belong to any of the three genera ; Rhizopus, Rhizomucor and Absidia.The acute infection is very commonly Rhinocerebral and originates in the nose and paranasal sinuses in patients with poorly controlled diabetes mellitus and metabolic acidosis.[2] It spreads quickly and can progress dramatically from the nose and paranasal area to the orbits and cranium in a matter of few days, if left untreated.[1] Survival is directly linked to early detection and prompt treatment.[3]

CASE REPORT

A 45 years-old woman was admitted in the Endocrinology ward of Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, in the month of December, 2001 for the management of diabetic ketoacidosis. The patient was a known case of Diabetes Mellitus on insulin therapy for the last 10 years but had not been regular with her antidiabetic medication. Five days prior to admission the patient had developed swelling of the left side of the face and left eye which progressively increased in size and within two days the patient had become drowsy and incoherent.

Examination at the time of admission revealed a critically-ill patient who was drowsy, incoherent and not well-oriented in time, space and person . The patient was tachypneic , with a fast irregular but feeble pulse, a blood pressure of 70/20mm Hg and marked dehydration. She had a putrid odour and was acidotic as confirmed by a low pH on ABG analysis.

The patient was put on I/V fluids, parenteral antibiotics and hourly insulin regimen but did not respond adequately to the treatment and developed swelling and discoloration of the left side of her face and eye. Over the ensuing three days, her condition deteriorated dramatically with swelling extending into the peri-orbital region and forehead. She started complaining of frontal headache and developed proptosis of the eyeball.

Cavernous sinus thrombosis was considered at this stage as a diagnostic possibility. The swelling of the face worsened further with localised loss of sensation of the left side of face, bleeding from left nostril and ocular palsy and finally gangrene of the face set in.

A diagnosis of facial herpes was considered and the patient was administered acyclovir, but again did not respond to the treatment. By this time, the necrotic process had spread into the paranasal sinuses, cheek, soft and hard palates and thorough surgical debridement was performed.

Swabs of the necrotic material were obtained from the nose and the hard palate, and microbiological examination was performed. Immediate wet mounts and KOH mounts were made from the necrotic material. Microscopic examination revealed the presence of broad non-septate hyphae, branching at 90 degrees. Fungal cultures were put on Saboraud's agar with and without antibiotics (cycloheximide 0.5mg\ml and chloramphenicol 0.05mg\ml).

Colonies on Saboraud's agar grew rapidly with the development of loose, cottony or wooly mycelium . Lacto-

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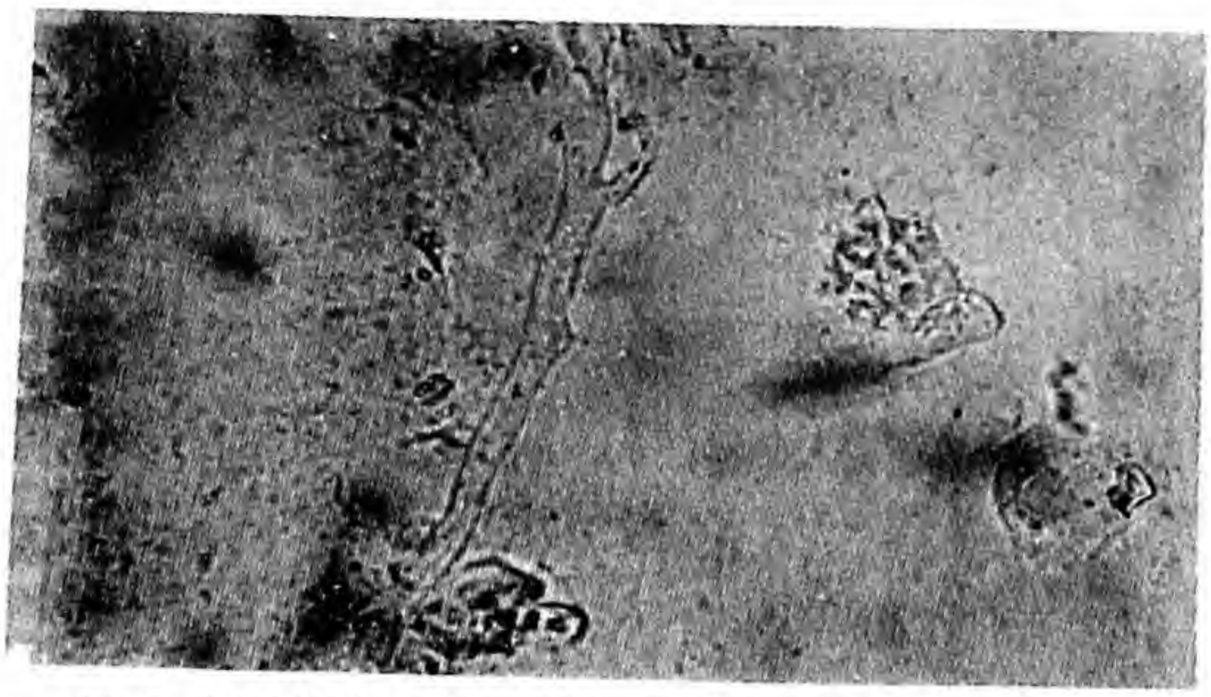

Fig.I: KOH Wet mount of the clinical sample showing broad aseptic hyphae with branching.

cotton phenol blue mounts were made which showed aseptate ribbon like hyphae with branching sporangiophores.The large ,spherical sporangium revealed numerous sporangiophores.Rhizoids were absent[4]

The diagnosis was reviewed and changed to Rhinocerebral mucormycosis owing to characteristic location of the lesions, underlying predisposing illness and most importantly the presence of characteristic broad hyphae on wet mount and KOH examination.

The patient was put on I/V amphotericin B in dose of 1mg/kg. The patient however did not respond to the treatment, became toxic and comatose and died on the fifth day of admission.

DISCUSSION

Despite therapy, mortality associated with this fulminant condition remains high, approximately 30-35% for the localized disease and higher mortality rates in disseminated cases i.e., close to 50%. Infection is acquired from nature with no person-to-person transmission. The portal of entry is highly variable. The fungus may gain access through lungs, PNS, GI tract, or damaged skin.[5,6] However, most of the organisms are airborne moulds. The underlying co-morbid factors include diabetic ketoacidosis (Rhinocerebral involvement), leukemia, immunosuppressive therapy (lung and disseminated infection), malnutrition (gastrointestinal infection), and burns or wounds (cutaneous invasion).[7]

A number of studies in the literature have documented diabetic ketoacidosis as the most common predisposing condition associated with invasive mucormycosis[2,3,8] but disease demographics are changing with the arrival of AIDS and the use of powerful immunosuppressive drugs.[9] Nearly one-half of recently reported cases comprise the rhinocerebral syndrome.[10]This is most frequently encountered in uncontrolled diabetes with diabetic ketoacidosis. The patient usually presents with fever and unilateral facial pain. There may be, subsequently, facial swelling with nasal obstruction and proptosis. The illness in our case also commenced with the same clinical presentation and pursued the same clinical course. There may also be invasion into the orbit, giving rise to orbital cellulitis and blindness and the brain causing hemiparesis.[9] The palate may also get involved in the course of disease process causing palatal ulceration/perforation. [11]The same sequence of events was witnessed in the case under discussion.

In time, the infection may disseminate producing infarction of major organs or limbs, in turn.[12]Its presentation can be confused with those of sinusitis, viral infection, diabetic ketoacidosis and cavernous sinus thrombosis.[1] At one time, the clinical course in the present case also raised the possibility of cavernous sinus thrombosis.

The diagnosis of this rare condition is often suggested by a combination of infection and widespread tissue destruction, localized to one of the typical sites of invasion.

Serology is commonly negative. The organisms are difficult to grow, even from the biopsy material. In establishing the diagnosis of this uncommon infection, biopsy of the necrotic material or skin scrapings is essential. Also early examination of smears and swabs by making wet mounts and KOH mounts and LCB mounts is essential. This is often the quickest way of arriving at a correct diagnosis. A delay in diagnosis is quite common owing to the rarity and unfamiliarity of the condition. In our patient, diagnosis was made within two days by microbiological examination but unfortunately the patient had passed beyond the stage of recovery despite rigorous antifungal therapy.

The hallmarks of a successful outcome in this aggressive infection, to a large extent, rely on early diagnosis by invasive procedures, immediate correction of the underlying predisposing condition, aggressive but thorough and repeated surgical debridement of the necrotic tissue and early rapid systemic coupled with a local antifungal therapy.[13] Amphotericin B is the only drug of proven clinical efficacy and should be employed in maximal therapeutic doses.

CONCLUSION

Mucormycosis is a serious life threatening condition striking patients with uncontrolled diabetes mellitus. Intravenous Amphotericin B is the only drug known to bring about a favourable outcome in this illness[14]. It should be administered as early as possible after making a diagnosis of mucormycosis to forestall the high mortality associated with this disease. A heightened awareness, with emphasis on early recognition, speedy diagnosis and prompt treatment may serve patients well. The residual facial defect can heal without undue disfiguration avoiding the need for a reconstructive surgery.

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SHY-DRAGER SYNDROME

S.K. Gupta; Vijay Kumar Verma; Ashok Parihar

Abstract: *Shy-Drager Syndrome is a well characterised severe form of multiple system atrophy and is manifested by parkinsonism, impaired autonomic functions resulting in postural hypotension, abnormal thermoregulatory sweating, disturbances of bladder & bowel control, impotency and gastroparesis. There are also features of somatic nervous system involvement in the form of external occular palsies, wasting of distal muscles & fasiculations and more widespread neurologic involvement along with pyramidal & cerebellar signs. We report here a case of Shy-Drager Syndrome who reported in the Emergency Department of Govt. Medical College Hospital, Jammu with attacks of giddiness & blackouts along with other features of parkinsonism, autonomic disturbances, laryngeal paralysis & pyramidal tract signs.*

Key words: *Shy-Drager Syndrome, Parkinsonism, Autonomic Nervous System.*

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Case Report

A 62 years old male, presented with attacks of sudden giddiness and blackouts while getting up from supine position, of one year duration. Attacks were so severe that the patient was even afraid of getting up from the lying down position. He had incontinence of urine and hoarseness of voice. There was no family history of such illness. He was non-diabetic and had no history of fever, convulsions or unonsciousness.

On examination he was having mask-like face, cog wheel rigidity of all the four limbs and glabellar tap was positive. Both planters were upgoing and there were no cerebellar signs. He had continuous dribbling of urine and also had laryngeal paralysis. Sweating was almost absent inspite of hot weather. His B.P. was 150/80 mmHg on lying down and while getting up it was 90/40 mmHg and the patient had to lie down immediately. While recording B.P. in standing posture, the patient used to become pale and there was turning of eye balls upwards but no change in pulse rate. His basal pulse rate was 88/minute and was regular. And all peripheral pulses including both carotids were normally palpable. Patient had irregular pupils and reaction to light was poor. X-ray chest and E.C.G. were normal. He was put on 24 hours cardiac monitoring without revealing any rhythm disturbances.

Routine texts viz., TLC, DLC, BUN, liver function tests, blood sugar were all within normal limits. STS was negative, CT scan head showed cerebral atrophy with dilated ventricles.

Physiological tests carried out like valsalva manoeuvre, cold pressure test and head up tilt at 45° failed to bring any change in B.P. or heart rate. Heart rate responses to deep breathing, hyperventilation and carotid massage also failed to show any change. Atropine injection did not bring any change in heart or pulse rate. Anhydrosis was confirmed by applying a starch-iodine mixture to the skin and by keeping the patient in a warm room. This did not bring any sweating.

Patient was treated with fludrocortisone acetate (1mg) twice weekly & elastic stocking to the legs. He was also given small doses of antiparkinsonian drugs. Patient showed improvement in his attacks of giddness and was able to walk with support. He was followed up for a period of two years.

Discussion:

Shy and Drager in 1960[1] described a syndrome where postural hypotension was associated with other autonomic disturbances like sphincteric disturbances, anhydrosis, impotency etc., with features of somatic nervous system involvement in the form of external occular palsies, parkinsonism, wasting of distal muscles, fasiculations, (multisystemic sclerosis)[2] and orthostatic hypotension which proved at autopsy to be associated with loss of intermediolateral horn cells and pigmented nuclei of the brain stem.[3] Vocal cord palsy is an important disorder causing dysphonia or even stridor and airway obstruction, requiring tracheostomy. Our patent had hoarseness of voice with laryngeal paralysis but did not require tracheostomy. Many of the patients have disturbances of urinary incontinence. The later abnormalities are of several types, involuntary detrusor contractions, the result perhaps of the loss of striatonigral inhibitory influences, inability to initiate voluntary micturition probably reflecting the

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degeneration of neurons in pontine & medullary nuclei & in the result of degeneration of sacral anterior horn cells[4]. Most patients present with autonomic dysfunctions alone and other neurologic manifestations usually develop within 5 years. Patients with striatonigral variant exhibit a form of parkinsonism in which bradykinesia and rigidity are more prominent than tremors. Our patient first had attacks of postural hypotension manifesting as vertigo and blackouts of one year duration followed by other features of parkinsonism but without tremors.

There is generally no treatment except for the postural hypotension which may respond to fludrocortisone, increased salt intake and elastic stockings.[5] The response to antiparkinsonian agents is usally disappointing.

To conclude, there are many causes of postural hypotension, but with a combination of urinary incontinence parkinsonian features, laryngeal paralysis and anhydrosis, one should always suspect Shy - Drager Syndrome.

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ANAESTHESIA AND MYASTHENIA GRAVIS

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Abstract: *Myasthenia gravis is an autoimmune disease characterised by production of antibodies against the acetylcholine receptors with the results that there is reduction in number of active receptors. The disease is frequently associated with morphological abnormalities of thymus. In young patients, thymic hyperplasia is common while thymoma is more frequent in elderly ptients. Adults with generalised myasthenia should have a transsternal thymectomy. A balanced anaesthesia which includes the use of muscle relaxants can be safety used, provided neuromuscular transmission is monitored. Myasthenic patients are sensitive to non-depolarising relaxants such as vecuronium and atracurium can be safety used. Postoperatively, ventilatory support may be required. Nearly 96% of patients benefit from thymectomy, 46% develop complete remission and 50% are asymptomatic or improve on therapy.*

Key Words: *Myasthenia graves, thymectomy, succinylcholine, pyridostigmine.*

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Preoperative

The patient was a 31 year old female who presented with a 3 year history of generalized weakness and easy fatigability.

3 years back patient was apparently alright when she started with drooping of Right upper eyelid, which progressively involved the left upper eyelid too. This was accompanied by easy fatigability, difficulty in swallowing both solids as well as liquids, and slurred speech. She was seen by a physician and labeled as Myasthenia Gravis, and started on Tab. Neostigmine - 10mg 4 hourly. After about 14 mcnths, patient stopped taking drugs and, again started with the same symptoms. Treatment was restarted, with the same dosage schedule, and patient was relieved of the symptoms. Patient again defaulted with the drug schedule, after 11 months; however, this time round, she had a more severe relapse. She presented with respiratory distress, which ws managed with Oxygen therapy, Tab. Neostigmine - 15mg 4 hourly, Tab. Prednisone (gradually increased from 10mg to 50mg/day) in the Critical Care Unit. Her symptoms started to worsen, when Tab. Prednisone was tapered after 1 month. Work up by a neurologist, involving repetitive EMG testing, was consistent with myasthenia gravis. A blood test showed her acetylcholine receptor antibody level to be 59 nanomoles/1 (normal is less than 0.04). Patient was put on Tab. Pyridostigmine- 60mg 8 hourly and continued with tab. Prednisone-20mg / day. Symptoms got controlled. Chest X-Ray revealed a soft mediastinal shadow, which was confirmed on CT Scan in the prevascular mediastinal compartment (Thymic Enlargement-?). Thymectomy was planne.

The patient was 160 centimeters and weighed 6 kilograms. Physical exam was unremarkable. Airway exam was Mallampati class I. All other laboratory data was unremarkable. A general anesthetic plan was discussed with the patient. She was advised to take pyridostigmine on the morning of surgery.

Intraoperative Course

A thymectomy via a median sternotomy was planned. The patient was brought to the operating room. Routine non-invasive monitors (including a peripheral nerve stimulator at the adductor pollicis muscle) were placed and 18g intravenous catheter was placed.

Cefazolin was given. The patient was preoxygenated. Induction was commenced usmg 150 micrograms buprenorphine, 300 miligrams sodium thiopental and 100 milligrams of succinylcholine.

Following muscle relaxation she was intubated without difficulty. Anesthesia was maintained with oxygen ard nitrous oxide (67;33) and halothane.

The patient did not regain a muscle twitch until 48 minutes after induction. At this time the patient was paralysed with atracurium besylate - 5 mgs. had two twitches after a 50 hertz tetanic stimulus. A second dose of atracurium was repeated at 22 mins, when response to the Train of Four stimulus was less than 75%. At 105 minutes she had regained all four twitches in a train of four stimulus with the ratio of the fourth and first twitch being 1:1. No further muscle relaxant was administered

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during the case. The surgery was completed in 120 minutes.

The patient was given 2.5 milligrams neostigmine and 0.5 milligrams glycopyrrolate. The patient demonstrated a good hand grip, a sustained head lift, a stable respiratory rate, and an unchanging end tidal carbon dioxide level. She was extubated in the operating room. She was then taken to the intensive care unit for further recovery and overnight monitoring.

Postoperative Course

The patient remained stable in the surgical ICU over night. She was started on his oral pyridostigmine immediately postoperatively. She showed no signs of weakness or respiratory distress over the next 24 hours. She received oral analgesics consisting of Diclofenac on a demand basis. On post-operative day one she was transferred to a regular floor bed. On post operative day eight she was discharged from the hospital in good condition.

Discussion

Myasthenia gravis is an autoimmune disorder characterized by a destruction of postsynaptic acetylcholine receptors at the neuromuscular junction. The factor that initiates and maintains the autoimmune response is not yet known.

The prevalence of the disease is approximately 25 to 125 cases per million population. Distribution is age and sex related, affecting females mostly in the second and third decades and men in the sixth and seventh decade. The presenting symptoms are weakness at the end of the day and fatigability that improves with rest. Facial and bulbar muscles are most commonly affected. The result of this weakness is diplopia, difficulty chewing and a characteristic flattened smile.

Physical findings are exclusively limited to the motor system, with no changes in reflexes or coordination. Diagnostic testing is conducted in the following order: anticholinesterase test (Tensilon test); repetitive nerve stimulation; an assay for anti-acetylcholine receptor antibody; single fiber electromyography.

A differential diagnosis would include congenital myasthenic syndrome, drug induced myasthenia, hyperthyroidism, Grave's disease, Eaton-Lambert syndrome, botulism, progressive external opthalmoplegia and intracranial mass lesions. These conditions must be excluded with the appropriate tests.

Myasthenia is graded functionally on a scale devised by Oserman (1971). Grade I involves focal disease (usually ocular muscles); Grade II a generalized mild; Grade II b generalized moderate; Grade III generalized severe and Grade IV involves a life threatening impairment of respiration.

Treatment is divided into anticholinesterase agents and immunosuppressive agents. Pyridostigmine is the most common of the anticholinesterase treatments. Anticholinesterases benefit most patients, but the improvement often dissipates with time.

The next line of treatment involves immunosuppression. This is most commonly achieved with corticosteroids (Prednisone). Benefit accures over 2 to 4 weeks and is maximal after 6 to 12 months. Azathioprine (Imuran), with its action on T-cells, is effective when corticosteroids are contraindicated or not tolerated. it takes up to a year to reach a therapeutic level. Side effects of azathioprine include fever, malaise and myalgias, The third immunosuppressive agent is cyclosporine (Sandimmune) which inhibits the production of interleukin -2 by the T-helper cells. Side effects include nephrotoxicity and hypertension.

Alternative therapeutic measures include plasmapharesis and intravenous immune globulin. The effects of plasmapharesis only last a few weeks. Intravenous immune globulin often brigns improvement in four to five days but lasts only weeks. Side effects include headaches, fluid overload and occasionally renal impairment. These are costly means of treatment.

Finally the most invasive modality of treatment is a thymectomy. The aim of a thymectomy is both to induce a remission and permit a reduction in the dose of immunosuppressive agents. Most patients between puberty and 60 years are suitable for a thymectomy. A thymectomy is never an emergency procedure. The patient should be in optimal condition prior to surgery. A transsternal approach allows the best exposure of the thymus, however a transcervical incision may also be used.

Consideratons for the anesthetic management would be the same for both thymic and non thymic surgery. Patients should be evaluated properatively by a neurologist. Medications should be checked and doses adjusted to optimize patient condition. The patient should be warned that there is a risk of controlled ventilation postoperatively.

Criteria that increase the likelihood of controlled ventilation in the post-operative period include (1) disease duration greater than 6 years, (2) non myasthenia related COPD, (3) pyridostigmine dose greater than 750 milligrams per day, (4) preoperative vital capacity less than 2.9 liters, (5) a transsternal approach.

The key to administration of muscle relaxants in myasthenic patients is to realize they have altered sensitivity to neuromuscular blockade. Myasthenics show an increased snesitivity to nondepolarizing agents (probably secondary to fewer functional acetylcholine receptors).

Myasthenics (whether on an anticholinesterase agent or not) show a resistance to succinylcholine. If a rapid onset of relaxation is desired, the dose of succinylcholine must be increased to at least 2 milligrams/kilograms. The

mechanism of resistance is unknown but may be related to the reduced number of (pre or post-synaptic) acetylcholine receptors at the neuromuscular junction.

Controversy exists as to whether preoperative pyridostigmine should be discontinued. Pyridostigmine will antagonize the degradation of succinylcholine and mivacurium, while increasing the dose requirements of the nondepolarizing agents. MG patients are resistant to the effects of succinylcholine (ED-95 is 2.6 times the normal in these patients). Clinically, however the use of succinylcholine has been without incident, with normal clincial doses producing adequate relaxation for endotracheal intubation and a normal recovery time, despite the occasionally reported early onset of phase II blockade.

In our patient we chose to continue with the anti-cholinesterase on the morning of surgery, to observe the effect of the same on the neuromuscular blockade produced by succinylcholine. The individual response of the patient to a specific relaxant must be titrated against the results of nerve stimulation. The potency of atracurium in myasthenics has been shown to be approximately 1.7 to 1.9 times normal. In our patient with a dose of 0.4 mg/kg (ED95*2) lasted approximately 100 minutes which is about 2.8 times the expected duration.

Maintenance can be achieved with nitrous oxide and a volatile anesthetic. Opioids can cause prologned effects on ventilation and hence should be used cautiously. The patient should always be given a reversal agent to antagonize the effects of the muscle relaxants.

Prior to extubation muscle strength should be evaluated. The patient's respiratory rate should be steady. They should demonstrate the ability to maintain a stable carbon dioxide level as assessed by either blood gas analysis or an end tidal value. patients may initially have good muscle strength only to fatigue post extubation. They should be monitored carefully in the postoperative period with provisions for rapid reintubation. Post operative pain can be managed with intravenous Opioids via patient controlled delivery or epidural opioids.

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AN IMPROVEMENT IN ETHANOLIZED HYDRATED RAT TECHNIQUE FOR ANTIDIURETIC AGENTS

Mir SA

Abstract: *Urine osmolality in ethanolized hydrated rat is exceedingly elevated, 355±39 mosmoles Kg^{-1} body water, as compared to control values, 43±3 mosmoles Kg^{-1} body water, from equally hydrated conscious rats. Evaporating the urine samples to dryness at 70°C, and reconstituting the residue to original volume with deionized water removes interference of ethanol with osmolality measurements. Urine osmolality of modified urine samples from ethanolized hydrated rats, 54±9 mosmoles Kg^{-1} body water does not differ significantly from control values. The modification renders the ethanolized hydrated rat technique suitable to differentiate antidiuretic agents on the basis of sites/modes of action.*

Key words: *Ethanol anaesthesia; urine osmolality; antidiuretic agents*

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Introduction

Ethanolized rat technique is standard method for assaying antidiuretic agents (Sturmer, 1968)[1]. Antidiuresis results from either reduction in GFR (Douglas, 1975; Erspamer et al 1973)[2,3] or reduction in free water clearance (Brazeu, 1975)[4]. It is parameter of urine osmolality measurement that would differentiate antidiuretic agents on the basis of these two modes/sites of action; it would be elevated with agents acting by enhancing renal tubular water reabsorption such as ADH or ADH-like agents including those which act by triggering endogenous ADH release such as pneumadin (Batra et al 1990)[5]. Presence of ethanol in urine in ethanolized hydrated rat renders such samples unsuitable for osmolality measurements. An investigation was mooted to study extent of variation in urine osmolality in ethanolized rat, and to introduce a simple modification to enable use of modified samples for monitoring urine osmolality.

Materials and Methods:

Wistar rats of either sex, 100 to 200 g body weight, non-fast were anaesthetized and hydrated by giving 12% (v/v) ethanol as 8% of body weight orally over 45 minutes. Urine samples were collected from catheterized urinary bladder over 4 hour observation period. Control urine samples were collected from conscious, trained, hydrated (given tap water as 8% of body weight) rats surgically prepared for the purpose with implanted catheter inside the urinary bladder. Osmolality of urine samples was measured by freezing point depression technique (Halbmikro Osmometer, Type M, Knauer). Aliquots of urine samples from ethanolized rats were evaporated to dryness at 70°C, reconstituted with deoinized water to original volume, and subjected to osmolality measurements.

Results and Discussion

Urine osmolality values in ethanolized hydrated rats were 783±151, 288±20, 239±6 and 426±111 mosmoles Kg^{-1} body water (n=6, each), respectively, at 0.5, 1,2 and 4 hour following anaesthesia under stable water diuresis 91 to 2ml min^{-1}). Average urine osmolality over 4 hour period remained very high, 355±39 mosmoles Kg^{-1} body water with high coefficient of variation (ca. 62%). Osmolality of modified urine samples, 54±9 mosmoles Kg^{-1} body water did not differ significantly from control values, 43±3 mosmoles Kg^{-1} body water from equally hydrated conscious rats under stable diuresis (n=6, $P > 0.05$).

Urine osmolality parameter determines site of action of antidiuretic agents. Agents that act like ADH to enhance renal tubular water reabsorption would enhance urine osmolality by raising osmolar clearance of urinary solutes, whereas agents that cause antidiuresis by reduction in GFR such as bombesin (Erspamer et al 1973)[3] would not significantly affect urine osmolality. Presence of ethanol in urine of ethanolized rat elevates urine osmolality and with high variability, and such samples as such are not suitable for measuring this parameter. Ethanol being volatile can be removed by evaporation without affecting solutes characteristically elevated by renal tubular water reabsorption. (e.g. sodium, potassium). The modification, evaporation and reconstitution to original volume with deionized water, renders urine samples suitable for monitoring osmolality parameter. The technique has proved indispensable for pharmacological characterization of

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pneumadin (Batra et al., 1990)[5] from mammalian lungs, and from neonatal rat intestines (unpublished), with respect to identifying sites/modes of action.

Acknowledgment

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UTILITY OF FINE NEEDLE ASPIRATION IN THE DIAGNOSIS OF THE NODAL PRIMARY NON-HODGKIN'S LYMPHOMA –(PART 1)

A.R.Khan; Shuab Omer; Sumia Rashid, Syed Besina

Abstract: *A study based on 6620 lymphnode aspirated over 11 years period (Jan. 1991- Dec. 2001) yielded 345 nodal lymphomas comprising of 255 cases of NHL and 90 cases of Hodgkin's lymphoma. The primary aim was to separate nodal lymphomas from other causes of lymphadenopathy in aspirates. However an attempt was made to subtype NHL using modified working formulation to accommodate some entities like mantle cell lymphoma and marginal zone lymphomas. The low grade NHL constituted 69 cases (27%) comprising of 62 cases of small lymphocytic lymphoma (SLL), 5 cases of lymphopplasmacytic lymphoma and one case each of mantle cell lymphoma and marginal zone lymphoma. In the intermediate grade there were 130 cases (51%) with 30- cases of mixed cell and 100 cases of large cell lymphoma. In the high grade group there were 56 cases (22%) comprising of 54 cases of Lymphoblastic lymphoma and 2 cases of Burkitt's lymphoma. In the low-grade group, there was excellent cytohistopathological correlation in SLL and lymphoplasmacytic lymphoma. There was only one case of false negative in SLL. 1 case diagnosed as SLL (SLL- CLL) later on 2nd opinion from two different lymphoma experts was reported as SLL –CLL and mantle cell lymphoma with leukemic phase .1 case of marginal zone lymphoma with villous lymphocytes diagnosed on FNA and PBF did not have tissue biopsy. In the intermediate grade of NHL, there were 5 cases of false negative which on histopathology proved follicular lymphoma(2 cases) and one case of SLL reported as reactive and mixed cell lymphoma (2 cases) In addition one case of large cell lymphoma on histopathlogy had earlier been diagnosed as poorly differentiated carcinoma metastatic to lymph node.*

This study proves that FNA is cheap and quick diagnostic procedure in the diagnosis of NHL and is well accepted by the clinicians and oncologists in the experienced hands, as the preliminary diagnostic approach in nodal lymphoma.

Key Words: *FNA, Nodal Lymphoma, Non Hodgkins Lymphoma (NHL), Hodgkin's Lymphoma (HL)*

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INTRODUCTION

Lymph node puncture is reported to have been done first by Greig and Gray[1] in 1904 for the diagnosis of trypanosomiasis in USA. This was followed by several reports on this subject from the same country [2-6] Cardoz [7] published a data in 1964 based on 1526 nodal aspirates and advocated its use in the diagnosis of primary neoplastic, non neoplastic and metastatic disease.

Some how it did not find much favour with American pathologists for many years, in spite of well accepted exfoliative cytology championed by George N Papanicolaou. Europe became the main attraction of FNA in 1950 onwards and publications from the Radiumhemmet of the Karolinska Hospital in Stockholm Sweden, caught the attention of pathologists world over . The two textbooks on the subject edited by Zajicek [8,9] bear a witness to work done over there. This institute has since produced numerous cytopathologists of high repute working in different countries world over.

Role of FNA lymph nodes is well accepted in reactive, infectious and metastatic disease. However its role in the diagnosis of primary lymphoma has been controversial[10,11] The main reason for this is the diverse lymphoreticular neoplasms and the changing classification on NHL over the last 25 years. However since late 1980's a number of publications have appeared to document the value of diagnosis and sub classification of non Hodgkin's lymphoma particularly when combined with immunophenotyping[12-19] . Authors present here their experience on the role of FNA in the diagnosis of primary nodal non-Hodgkins lymphoma based on 6620 lymphnode aspirates.

MATERIAL AND METHODS

This study is based on 6620 lymph node aspirations, conducted over 11 year period (Jan. 1991 to Dec. 2001) in Department of Pathology Govt. Medical College Srinagar and a referral clinic of one of authors (ARK) . More than 98% aspirations were done on an outpatient basis. One of the authors (ARK) was the principal aspirator. A 10 ml or 20 ml disposable plastic syringe with and without a syringe holder and 22-24 G disposable needles were used. Deep-

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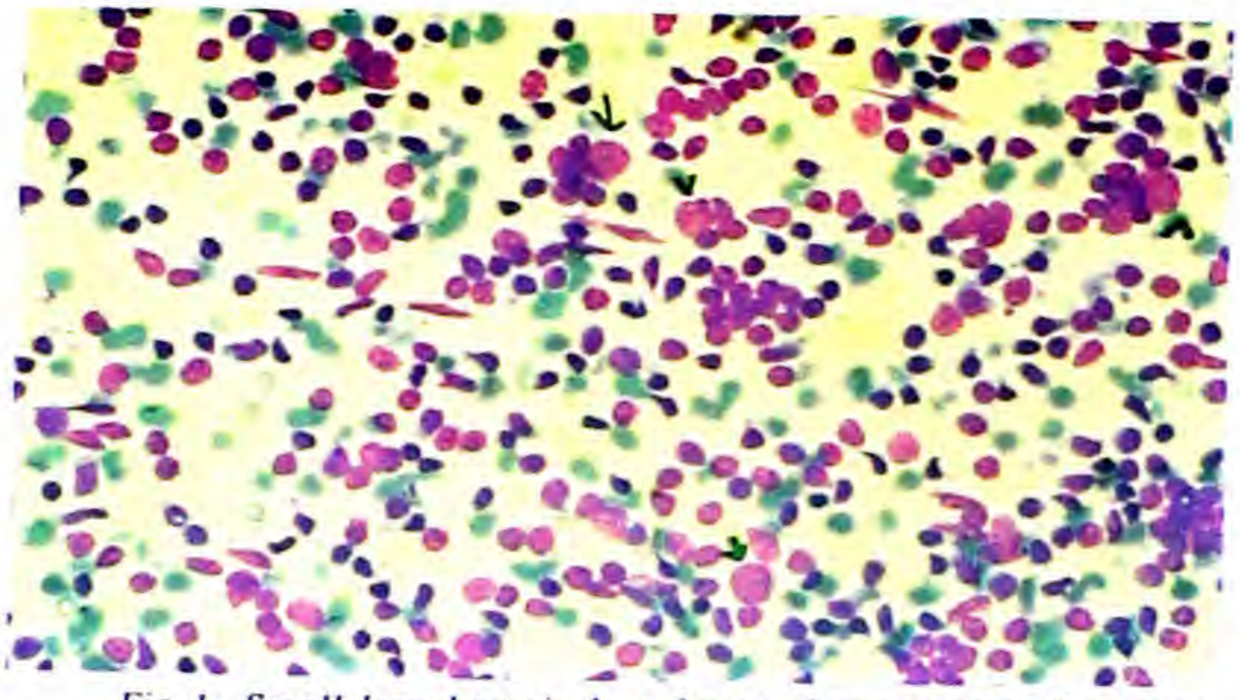

Fig 1: Small lymphocytic lymphoma shows sheets of mature lymphocytes with scattered larger lymphoid cells (arrowheads). MGGx400.

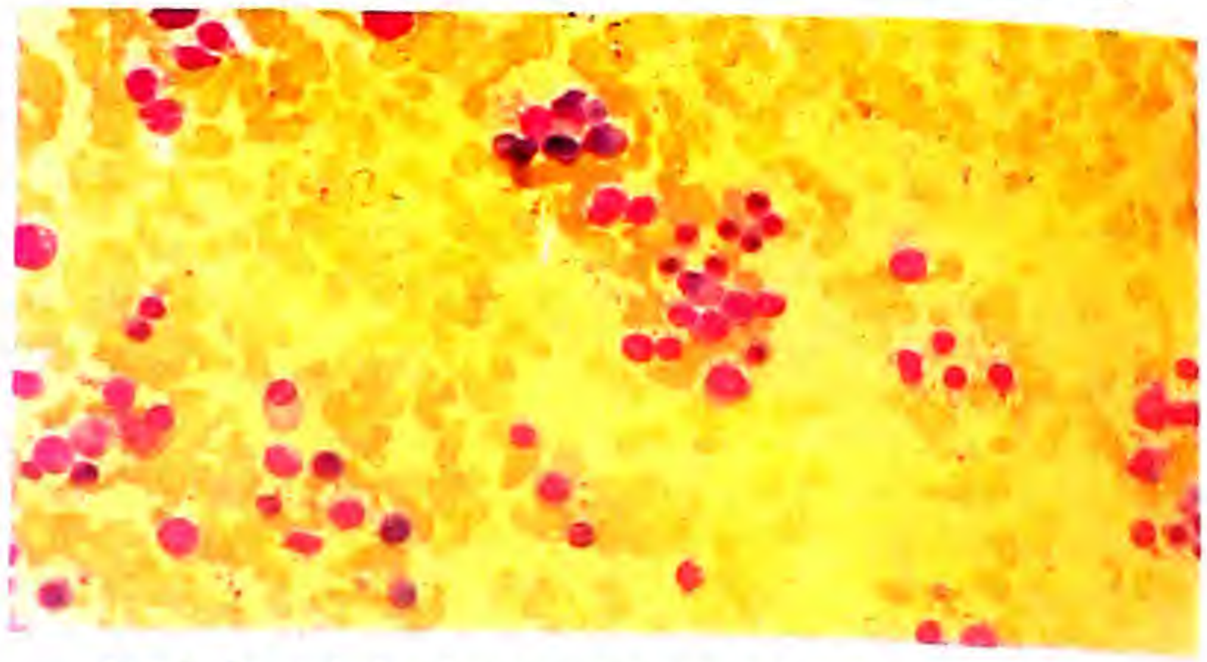

Fig 2: Lymphphoplasmacytic lymphoma shows small lymphocytes intermixed with slightly larger cells lymphoplasmacytes (arrowheads) with more abundant cytoplasm and eccentric nuclei. MGGx400.

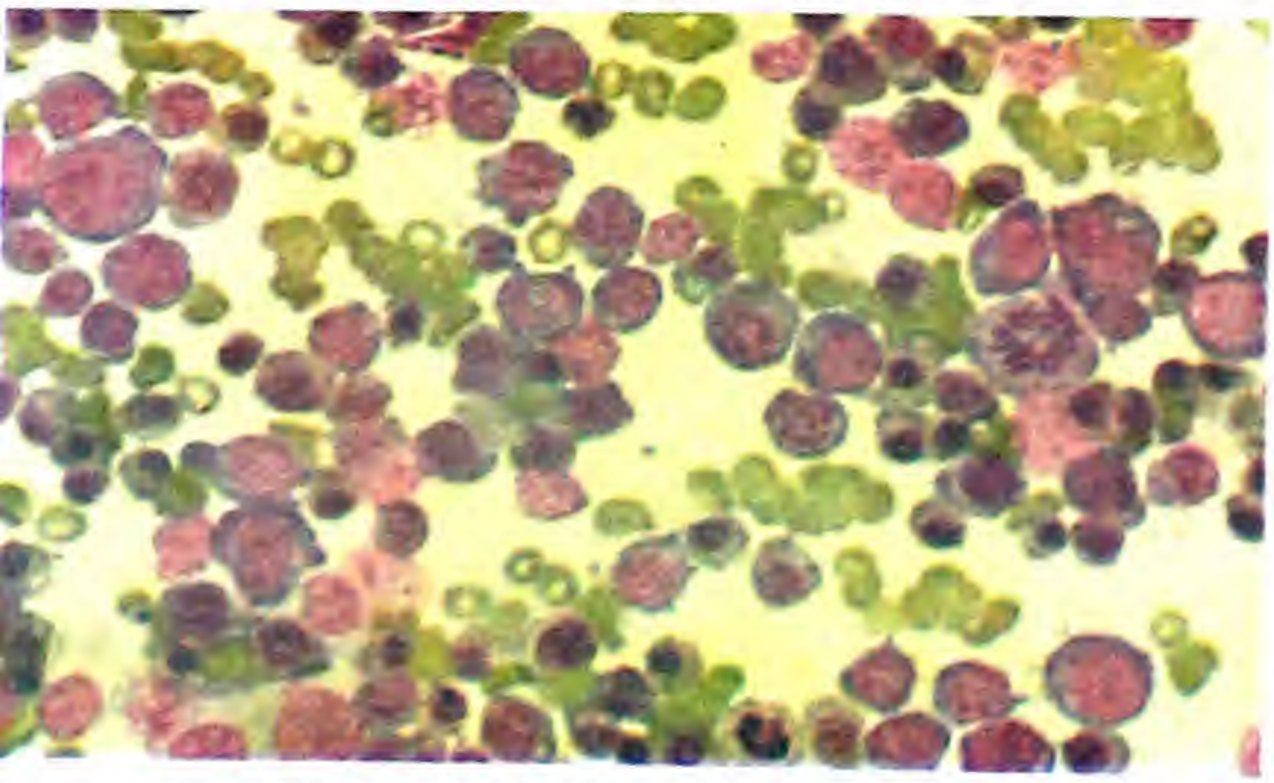

Fig 3: NHL large non cleaved cell. MGGx400.

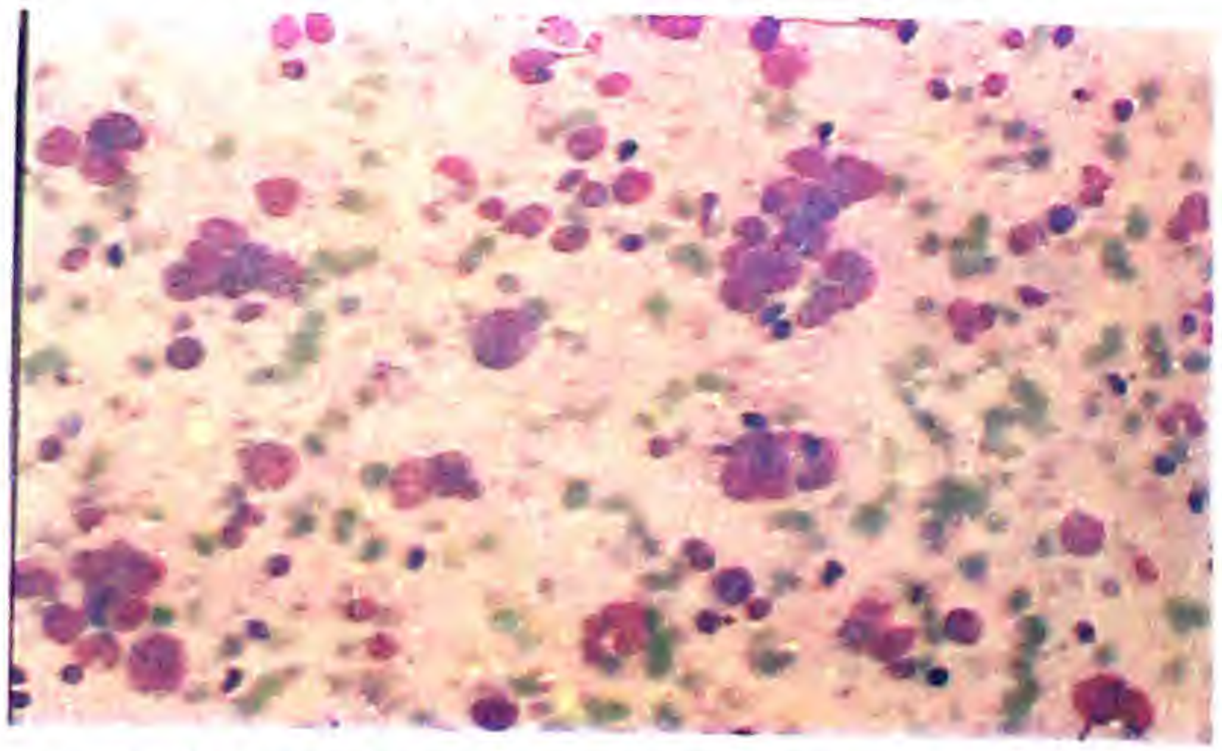

Fig 4 : Large cell lymphoma cleaved cell shows clustering of lymphoid cells. MGGx400.

seated nodes were aspirated under USG and CT guidance using 22G long needles. Material aspirated was spread over 3-6 slides. Air dried, MGG stain was used in all cases, wet alcohol – fixed H & E stain in some cases and PAS in selected cases only.

TABLE 1
FNA Lymphnode results
(Jan1991-dec2001)

Cytological Dx	Patients No.	Percentage
1 Reactive/Infectious (nontuberculous)	3628	54.80
Tuberculous	1994	30.12
Metastatic Malignancy	490	7.40
Lymphoma(primary nodal)	345	5.21
Inconclusive	163	2.46
Total	6620	100%

P.S Extra nodal lymphomas and those reaspirated for residual and relapses are excluded.

All the patients, whose smears were positive or suspicious for lymphoma, were subjected to lymphnode excision biopsy. Also subjected to excision biopsy were those cases with negative smears but suspicious on clinical grounds.

The primary aim of the FNA of lymphnodes in this study was to decide between lymphomatous, reactive and metastatic disease. An attempt was made to subtype NHL using Working Formulation[20] with some modifications to accommodate some entities like mantle cell lymphoma and marginal zone B cell lymphoma.

CRITERIA FOR CYTODIAGNOSIS WERE:

Low grade lymphoma:

Small lymphocytic B cell lymphoma (SLL): Shows sheets of lymphocytes with round nuclei, coarse clumped or blocky chromatin, no nucleoli and regular nuclear membrane and scanty cytoplasm. A second population of larger cells so called prolymphocytes and paraimmunoblasts with round nuclei vesicular chromatin and solitary distinct nuclei are present in small numbers.

Lymphoplasmacytoid lymphoma (LPL): Shows sheets

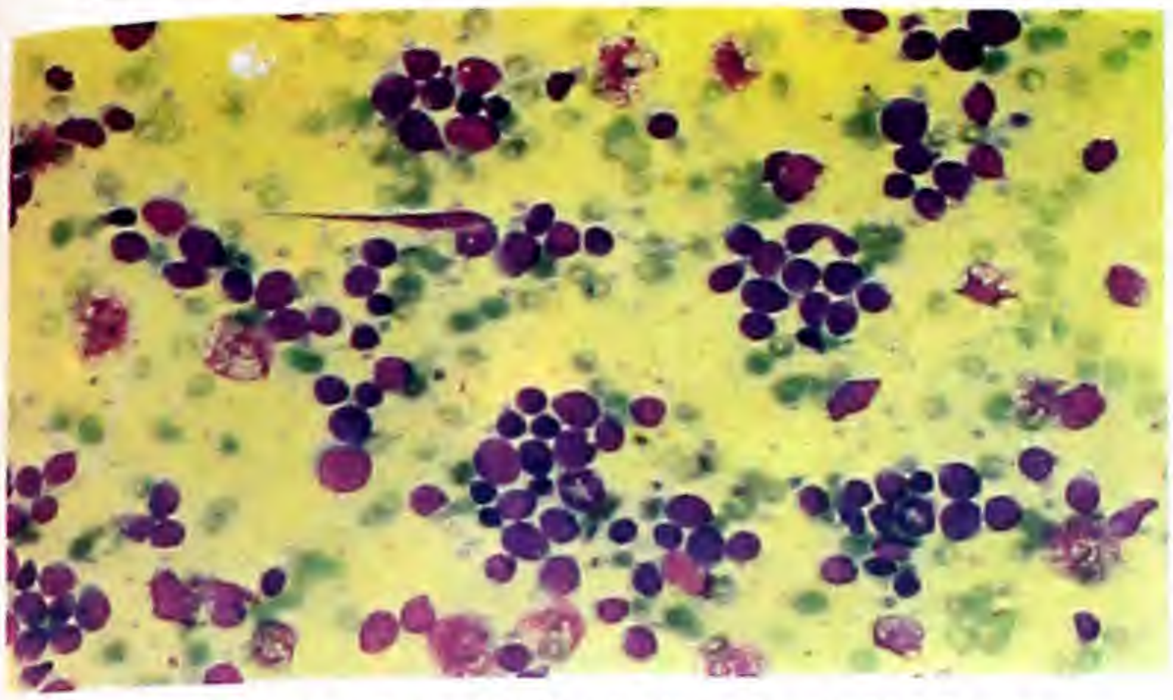

Fig 5 : Lymphoblastic lymphoma.MGGx400.

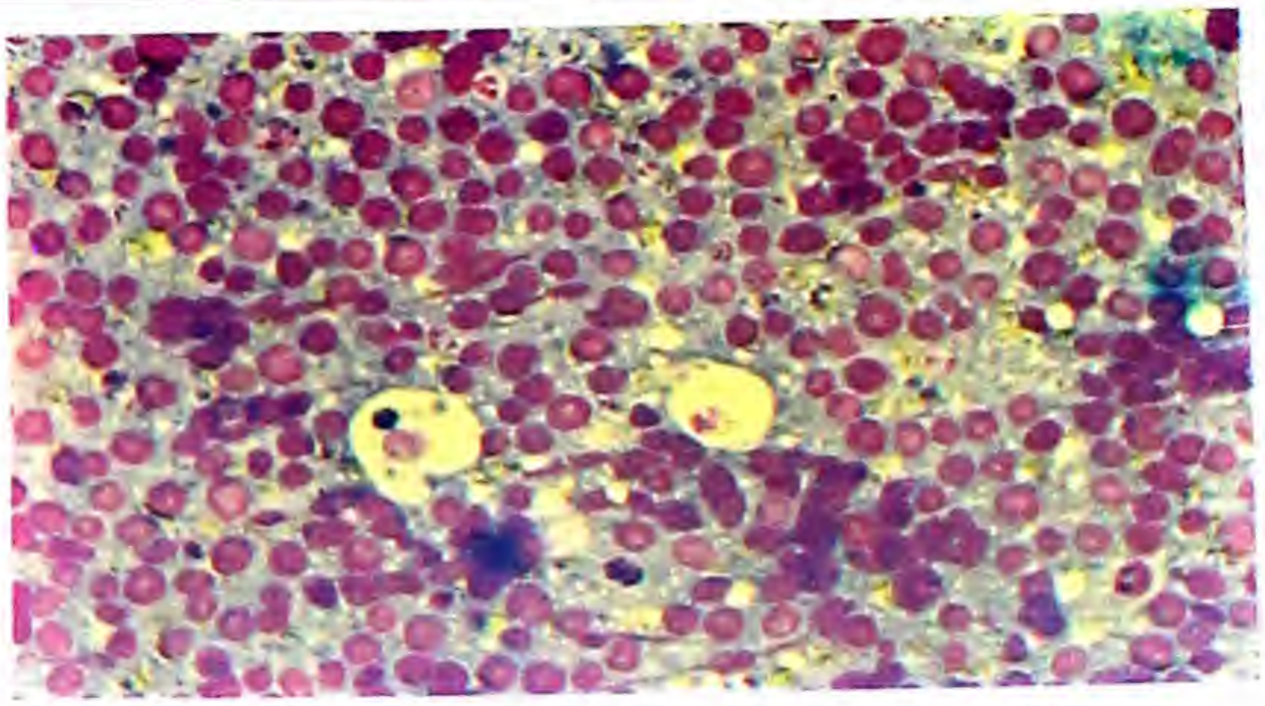

Fig 6 : Burkitt's lymphoma shows medium sized lymphoid cells with tangible body macrophages.MGGx400.

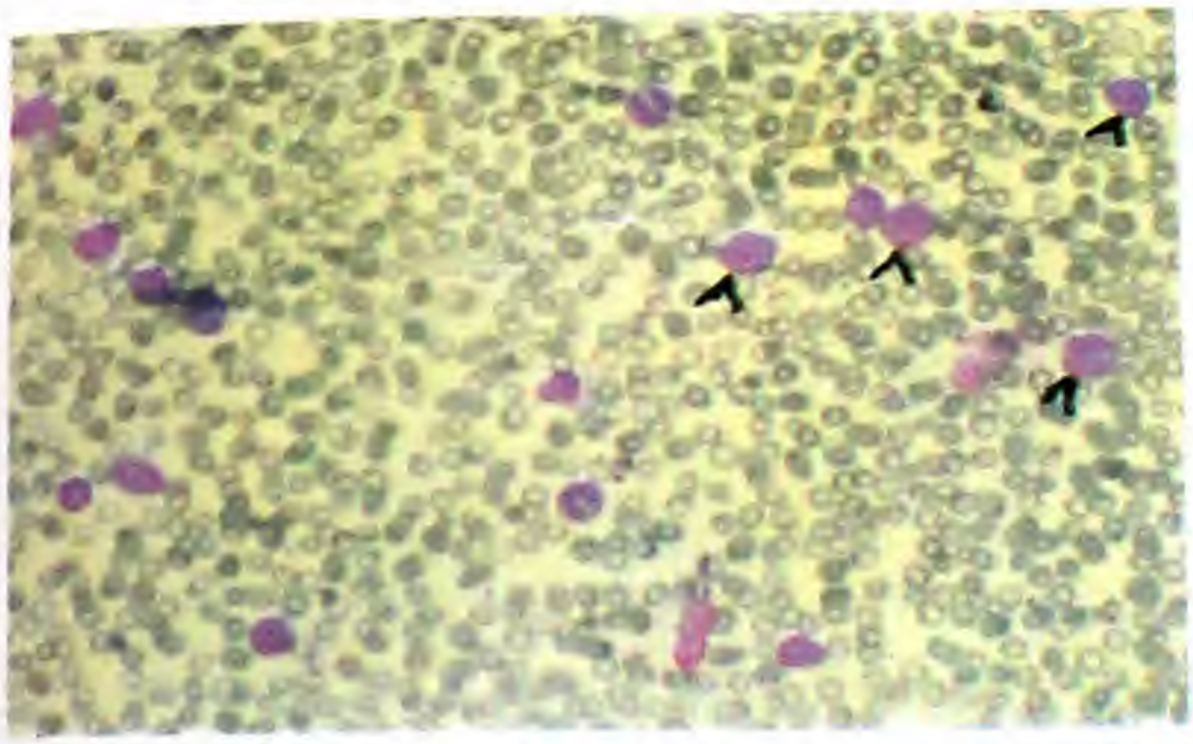

Fig 7 : NHL large cell with leukemic coversion. PBF shows large lymphoma cells (arrowheads) with occasional lymphocytes and neutrophils.Leishman stain x400.

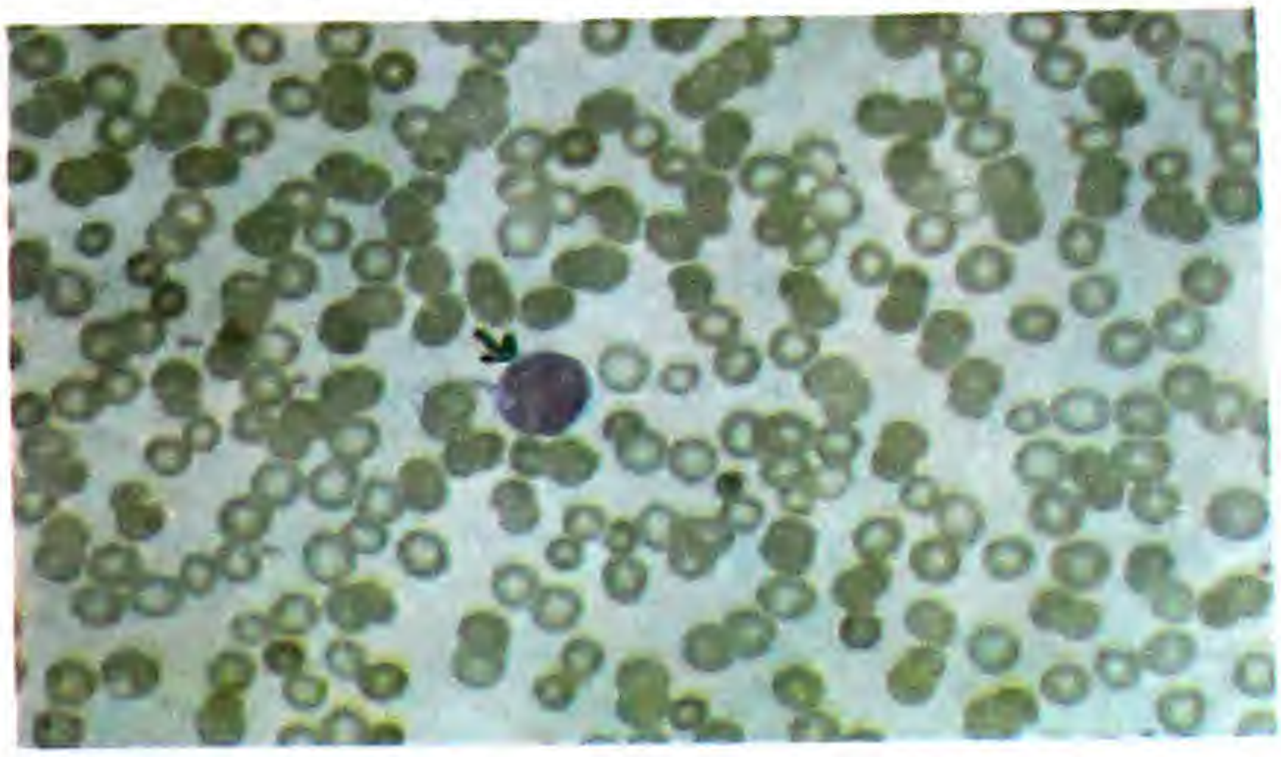

Fig8: PBF with villous lymphocytes (arrowhead) and one lymphocyte ,no platelet seen. Smear showed pancytopenia. Leishman stain x 400.

of small lymphocytes, plasmacytoid cells and occasional plasma cells. Many plasma cells should lead to consideration of macroglobulinemia.

Marginal Zone (MZL)/ monocytoid B cell lymphoma: Shows monomorphic population of small to medium sized cells with round nuclei condensed chromatin, indistinct nucleoli and more abundant cytoplasm. Variable number of plasmacytoid lymphocytes and mature plasma cells may be present.

Table 2
FNA 345 cases of Nodal lymphomas
(Jan1991-dec2001)

	Type	No. of cases	%age
1.	Non-Hodgkins Lymphoma	255	74%
2.	Hodgkins lymphoma	90	26%
3.	Total	345	

Mantle cell lymphoma (MCL): Shows monotonous population of small to medium sized lymphoid cells with irregular nuclear outline, less condensed chromatin than small lymphocytes and scanty cytoplasm.

Table 3
FNA-255 cases of nodal NHL Age and Sex Distribution

Age(year)	Male	Female	Cx	Ax	Ing	Abd	Media-stinal
1-9years	14	7	11	1	1	7	
10-14years	10	1	7	1	2	1	1
15-19years	12	4	14	0	0	2	
20-29years	16	8	22	1	0	1	
30-39years	18	8	22	2	2	0	
40-49years	25	5	19	3	6	2	
50-59years	37	20	33	14	7	3	
60-69years	33	12	34	9	1	1	
70-79years	17	4	12	7	2	0	
>80years	2	2	3	0	1	0	
Total	184	71	177	38	22	17	1

Follicular lymphoma grade 1 and 2 Shows predominantly small cleaved cells slightly larger in size than small lymphocytes with less condensed chromatin, indistinct nucleoli, cleaved nuclei and scanty cytoplasm. Variable number (<25%) of large non cleaved cells are also

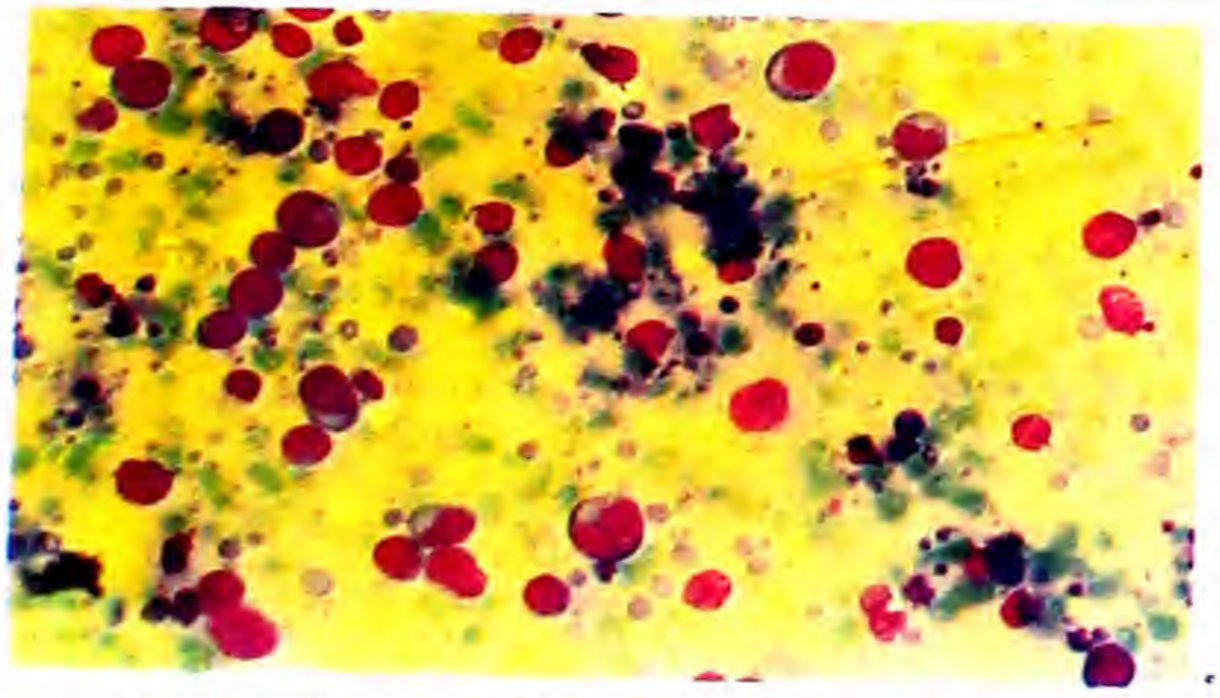

Fig 9 : Follicular lymphoma large cell (grade 3) MGG x 400.

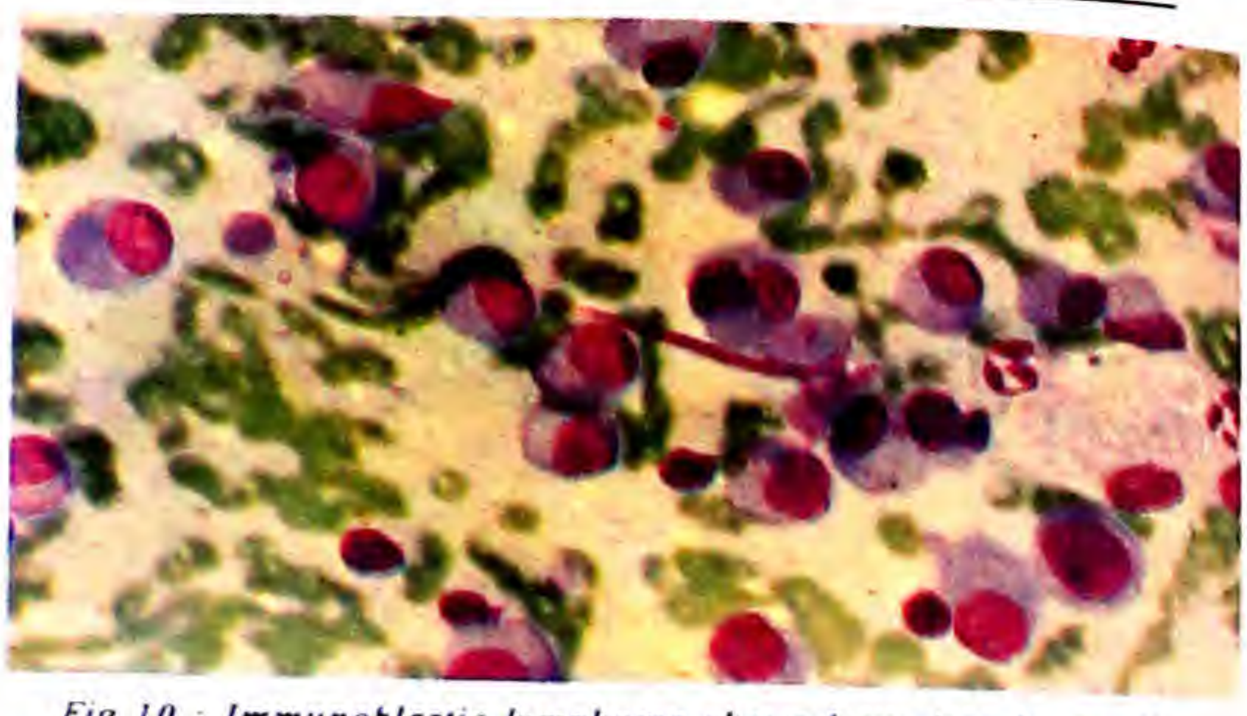

Fig 10 : Immunoblastic lymphoma shows large lymphoid cells with eccentric nuclei, prominent nucleoli and abundant cytoplasm MGG x 400.

Table 6: FNA 255 cases of nodal NHL Age and Sex Distribution of NHL- Subtypes (FNA Jan 1991-Dec 2001)

Age (Yr.)	Low grade lymphoma						Intermediate grade		High Grade			
	SLL		Lymphoplasmacyctic				Mantle cell		Lympho blastic		Burkitts	
	M	F	M	F	M	F	M	F	M	F	M	F
1-9	0	0					0	1	12	6	2	
10-14	1	0					0	0	9	1		
15 19	1	0					4	2	7	2		
20-29	4	2					7	3	8	3		
30-39	5	1					11	7	1	1		
40-49	8	1			1		13	5	1	0		
50-59	17	8	2				17	11	0	1		
60-69	6	1	2	1			24	8	1	1		
70-79	5	2					12	1	0	0		
>80	0	0					2	2	0	0		
Total	47	15	4	1	1		90	40	39	15	2	

present (Grade I), 25-5% laye cells in grade 2 F. lymphomas

Intermediate grade Lymphoma:-

This category would include grade 3 follicular lymphoma, diffuse large cell lymphoma, peripheral T cell lymphoma and anaplastic lymphoma. The large cleaved cells are two to three times or more in size than small lymphocytes with cleaved nuclear membrane, pale chromatin small indistinct nucleoli and scanty lightly basophilic cytoplasm. The large noncleaved cells are of similar size with round nuclei, a well defined smooth nuclear membrane, two to three nucleoli some close to nuclear membrane and moderate pale basophilic cytoplasm. Immunoblasts are of similar size withy more abundant basophilic (Bcell) or light (Tcell) abundant cytoplasm and eccentric round vesicular nuclei and prominent (B cell) or small nucleoli (T cell). Anaplastic lymphoid cells are larger with bizarre (B cells) or horseshoe shaped nuclei (Tcell). These cells maybe present in various mixtures in large anaplastic lymphomas. Mixed cells lymphomas generally contain 25 to 50 % large cells whereas larger cell lymphomas contain more than 50% large cells. This arbitrary division is not easily reproducible. Also included in this are T cell rich or histocyte rich B cell lymphoma where large lymphoid (B cell) are less than 50 % in number.

Table 4
FNA 255 cases of nodal NHL (Quality of report)

1. Diagnostic ——— 239cases
2. Suggestive/Suspicious——10 cases
3. False negative ——— 6 cases (includes one case of lymphoma misdiagnosed as metastatic carcinoma)
4. False positive ——— nil

High grade lymphomas:-

This group includes lymphoblastic and small non cleaved Burkitt's and Burkitt's like lymphomas. Lymphoblastic lymphomas shows sheets of small to medium sized cells with scanty basophilic cytoplasm and round nuclei with

fine chromatin, indistinct nucleoli 1-2 and well defined nuclear membrane. Variable number of mitosis are present. Burkitt's lymphoma shows medium sized cells with more abundant basophilic and vacuolated cytoplasm (in MGG stain), round nuclei with 2-3 nucleoli, many mitotic figures and variable number of tingible body macrophages. Burkitt's- like lymphoma are similar in morphology apart from variation in the size of tumor cells. Lymphoglandular bodies (LGB) are present in variable numbers in all lymphomas. Tingible body macrophages (TBM) though a prominent feature of Burkitt's lymphoma, can be present in any aggressive lymphoma & also in reactive nodes.

Table 5
FNA 255 cases of nodal NHL sub typing using WF

		Total	%age
1. Low grade lymphoma—		69	27
	M	F	
A) Small lymphocytic	47	15	
B) Lymphoplasmacytic	04	01	
C) Mantle Cell	01	00	
D) Marginal Zone	00	01	
		Total	%age
2. Intermediate grade lymphoma		130	51%
	M	F	
a) Mixed cell	21	09	
b) Large cell including large cell centroblastic, large cell centrocytic Immunoblastic and anaplastic and large cell peripheral T cell lymphoma	69	31	
		Total	%age
1. High grade lymphoma		56	22
	M	F	
a) Lymphoblastic	39	15	
b) Burkitts	02	00	

Leukemic phase was recorded in
1. 14 cases of SLL in the beginning after FNA diagnosis
2. 1 cases of MCL in the beginning
3. 3 cases of LCL in terminal phase of disease
4. 3 cases of LBL after FNA diagnosis

RESULTS:

Fine needle aspiration results based on 6620 lymphnode aspirations conducted over 11 years period are shown in table 1. Primary lymphomas constituted 345 cases (5.2%). In addition 36 cases of known lymphomas under treatment were reaspirated either for residual or recurrent disease or staging purposes. Extra-nodal non-Hodgkin's lymphomas diagnosed by FNA over this period are not discussed in this communication. Age, Sex, and anatomical distribution of non-Hodgkin's lymphomas, comprising of 255 cases (76%) of nodal lymphoma is shown in table 2. Thirty-two cases (> 13%) of non- Hodgkin's lymphoma occurred in children aged 1-14 years. In adults over the age of 14 years, most cases were seen in the 5th –7th decades. Male to female ratio was > 2.5 : 1 in both children and adults. Cervical nodes 177 in number (69%) were the most frequent sites of FNA followed by axillary, inguinal and abdominal nodes. There was only one case from mediastinum (table 3).

Table 4 depicts the quality of smears. Thus a clear-cut diagnosis was offered in 239 cases (>95%) and a suggestive / suspicious of non-Hodgkin's lymphoma in 10 cases. There were 5 cases of false negative and one case of misdiagnosis of carcinoma for lymphoma. Out of 239 cases diagnosed on FNA all were confirmed as non-Hodgkin's lymphoma on nodal excision biopsy. Out of 10 cases with a suggestive / suspicious of NHL on FNA, all the cases were subsequently confirmed as NHL on histopathology. There were however, 5 cases of false negative, which were reported as reactive on FNA and a subsequent histopathology of excised nodes proved to be small lymphocytic lymphoma (1 case), follicular lymphoma (2 cases) (Fig. 3, 13) and mixed cell lymphoma (2 cases).

Patients diagnosed as non-Hodgkin's lymphoma were classified as low grade, intermediate grade and high grade according to Working Formulation which was modified to accommodate some entities like mantle cell and marginal zone lymphoma. A subtyping of NHL on FNA, attempted is shown in table 5. Low grade NHL constituted 69 cases (27%), intermediate group 130 cases (51%) and high-grade NHL 56 cases (22%).

Low grade lymphomas: - In this group, SLL was the most common type. Age, Sex and anatomical site distribution is shown in table 6. Six cases were recorded below the age of 30 years and the youngest patient was 14 years old male with lymphnode enlargement on right side of neck. The lymphnode excision confirmed the diagnosis by 2 groups of pathologists independently. Male to female ratio of SLL group was 3:1. Smears were generally cellular composed of small round cell lymphocytes, intermixed with occasional prolymphocytes / para-immunoblasts. Lymphoid cells were generally dispersed but clustering was seen in addition in some cases mimicking small cell carcinomas (fig. 1) 14 cases of SLL showed a leukemic phase at the time of diagnosis (SLL-CLL). There were 4 cases of lymphoplasmacytic lymphomas composed of mature lymphocytes and lymphoplasmacytes and occasional plasma cells (Fig.2). However in one of these, there were also many plasma cells. This case on further investigation proved to be Waldenstromas macroglobulinemia [21]. There was one case of a 42 yr old male, with moderate splenomegaly, minimal cervical lymphadenopathy and peripheral blood lymphocytosis. He was diagnosed as low grade lymphoma (SLL-CLL). The material of this case was referred to two lymphoma experts who made the diagnosis of SLL-CLL and mantle cell lymphoma with leukemic phase

respectively. However only B cell associated antigens and CD5 alone were used which were all reactive. This case was treated as mantle cell lymphoma with incomplete remissions and death within 2 years. Another case of 59-year-old female who presented with moderate splenomegaly and minimal cervical lymphadenopathy was aspirated at both sites. A FNA diagnosis of low-grade lymphoma was made. Peripheral blood examination showed pancytopenia with villous lymphocytes in peripheral smear (Fig. 8) Diagnosis of marginal zone B cell lymphoma with villous lymphocytes, was made. Patient however refused further investigation and was lost to follow up.

The Cyto-histopathological correlation of SLL and lymphoplasmacytic lymphoma was excellent.

Intermediate grade lymphoma:-

This aggressive lymphoma group was the largest group with 130 cases constituting a little over more than half the cases of NHL in the study. Age and sex distribution in the table shows that only one case of large cell lymphoma was seen in age group 1-14 yrs. Most cases (40 %) were in 6th-7th decade. Male to female ratio was 2.25:1. Smears of this group (Fig 4,5,6,7& 14) were generally cellular with well dispersed tumour cells, many lymphoglandular bodies (LGB) and a variable number of tingible body macrophages (TBM) but follicle center cell (FCC) fragments were absent. Cell clustering was not uncommon especially in large cleaved cell predominant lymphomas (Fig. 4). This large cell predominant group generally is easy to interpret. However problems may arise at times in distinguishing these from metastatic large cell carcinomas especially in the head and neck region. The mixed cell lymphomas are a heterogeneous group difficult to subtype on FNA and mimic reactive lymphadenitis. Thus in this study there were 10 cases, where diagnosis was only suggestive/suspicious which were confirmed later as non-Hodgkin lymphoma on excision biopsy of the node. There were in addition 5 false negative cases, 4 diagnosed as reactive node and 1 misdiagnosed as metastatic carcinoma poorly differentiated.

Three cases in this group showed leukemic conversion in the terminal phase of illness (Fig. 7).

High-grade lymphomas: -

There were 56 cases (22%) in this group comprising of 54 cases of Lymphoblastic lymphomas and 2 cases of Burkitt's lymphoma .Age and sex distribution as seen in table 6 shows that both the cases of Burkitt's lymphoma occurred in male children in the first decade. Lymphoblastic lymphoma showed a wide age range though, most of the cases (>90%) occurred in first three decades. In children below the age of 14 years lymphoblastic lymphomas accounted for most (87.5%) of childhood nodal non-Hodgkin's lymphomas. Three cases in children showed leukemic phase on investigation after FNA diagnosis (LBL-ALL). Lymphoblastic lymphoma smears were fairly cellular with dispersed monomorphic cells and variable number of mitotic figures and lymphoglandular bodies were present (Fig. 5). Burkitt's lymphoma smears were also cellular with dispersed and clustered monomorphic cells medium sized, many lymphoglandular bodies and mitotic figures (Fig. 6). This group of high-grade lymphomas showed virtually 100% Cytohistopathologic correlation.

Discussion.

Fine needle aspiration is now considered the first step in the work up of patients with lymphadenopathy. Diagnostic role of FNA is well established in lymphnode infectious and metastatic disease. FNA diagnosis of primary lymphomas however has been controversial but is now widely accepted though recognizing its limitations [7,11,12,15,19,22]. This controversy is accounted for by a number of reasons. The foremost being the wide spectrum of NHL sub types and ever-changing classification over the last 25years. Other reasons are partial involvement of the lymphnodes and sampling error, lack of availability of tissue architecture on FNA, small nodes, difficult sites, sclerosing non–Hodgkin's lymphoma, composite lymphomas, peripheral T cell lymphomas and marginal zone lymphomas . Diagnostic limitations are further governed by the experience of aspirator as well as experience of interpreter.

Working Formulation[20] on NHL classification has been in use for nearly 2 decades now; though it is being generally replaced by REAL[23] and WHO[24] classifications in laboratories with facilities for ancillary studies. Working formulation in smears suffers from limitation of architecture and depends on morphology alone. This has been overcome to a great deal by immunophenotyping. Some authors claim a specificity and predictive value of over 90% with immunologic studies and morphology[25]. However when morphology and immunophenotyping is inconclusive accurate classification requires cytogenetics and DNA analysis[26]

The present study is a report based on more than 35000 FNAs including 6620 lymphnodes yielding 345 lymphomas (255 NHL and 90 HL). However here in this presentation only FNA diagnosis of 255 cases of nodal NHL is discussed. In low-grade lymphoma category the SLL showed high cytohistopathological correlation with one case of false negative report, in young male with multiple nodes in left axilla. This could probably be attributed to non-representative sample. Another case diagnosed as low grade lymphoma (SLL-CLL) was referred to two lymphoma experts who reported it as SLL-CLL and mantle cell lymphoma. Patient was treated as mantle cell lymphoma with incomplete remissions and death from uncontrollable disease within 2 years of diagnosis. There were also 5

cases of lymphoplasmacytic lymphoma, one of these on investigation proved to be a case of Waldenstromas macroglobulinemia[21]. The other four, were confirmed as lymphocytic lymphoma with some plasmacytoid differentiation. One case, a 59years old female was labeled from FNA of few small peripheral nodes and peripheral blood examination as marginal zone lymphoma (spleen and lymphnode) with villous lymphocytes (Fig 8). However patient was lost to follow-up without biopsy confirmation.

In the Intermediate grade category, there were two broad subgroups of mixed lymphoma and large cell lymphoma (Fig.5,6). There is an arbitrary division between these two on FNA smears. These two categories of mixed and large cell lymphoma include more than one subtype. Thus the large cell category including large non-cleaved, large cleaved cells, Immunoblastic and pleomorphic large cell type together constituted more then 50% of NHL in this study. Histopathologic correlation as a broad group in the intermediate category was generally good. Smear of four cases diagnosed as reactive on FNA, on review could at the most be considered as suspicious. However one case misdiagnosed as metastatic carcinoma on review was a clear-cut case of large cell non-Hodgkin's lymphoma. Sixth case of SLL was reported as reactive has been already been discussed above. In all there were 14 cases, out of 130 cases where the diagnosis was either in doubt or negative or a misdiagnosis. Thus this group can pose difficulties on FNA on pure morphology without immunologic or other ancillary studies.

In the high grade group with 54 cases of lymphoblastic lymphomas and 2 cases of Burkitt's lymphoma, cytohistopathologic correlation was consistent. It is the easiest category to identify at least as high-grade tumors on cytology irrespective of phenotyping. However lymphoblastic lymphoma may mimic small cell carcinoma in adults & blue cell tumours in children.

In summary, therefore, it can be concluded that FNA has a first step diagnostic role in primary non-Hodgkin's lymphoma apart from its diagnostic role in residual and recurrent disease or staging .It is cheap, quick and reliable in the experienced hands. From the data itself it is clear how well it has been accepted by the clinicians and oncologists alike. FNA morphologic diagnosis of NHL in experienced hands can be safe even in absence of Immunophenotyping and other ancillary studies. Further those cases where FNA is non-commensurate with clinical picture excision biopsy should be undertaken to avoid delay in the diagnosis. Experience of the aspirator and interpreter of course is most important. In case of deep nodes like intraabdominal or intrathoracic region or where serious illness does not permit surgical intervention, clear cut diagnosis of NHL on FNA by an experienced cytopathologist is adequate to permit the treatment without biopsy confirmation.

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MANUAL SMALL INCISION CATARACT SURGERY (SICS)

MQ Keng; AR Nasti; SB Khanday

The surgery of cataract dates back to 1000 B.C. and has evolved over time to emerge as perhaps the most effective surgical procedure in all of Medicine[1]. Modern cataract surgery aims at the visual rehabilitation in a minimally invasive manner.

Though phacoemulsification has emerged as the "state of art", appropriate technology rather than the latest high technology should be the watchword. Considering the resource crunch in the developing countries, the cost and maintenance of such equipment put it beyond the availability to most patients, which makes it imperative to emphasise on 'Manual SICS', which is cost effective and safe surgery with visual results as good as in phacoemulsification[2].

Various advantages of SICS are;-

- Can be performed as an OPD procedure
- No stitches/ one stitch occasionally
- Quick visual rehabilitation
- Less surgically induced astigmatism.
- Fever visits for follow up care.

The added advantage with SICS is the possibility of performing astigmatically neutral incisions.

Thus SICS has made cataract surgery both a therapeutic and a refractive procedure.[3]

The role of newer technologies like Nd: YAG Laser Phacophotofragmentation, 1053-nm picoscond laser phacophotofragmentation, Er: YAG (2.94 um) Laser photoablation, excimer laser photoablation (especially 308-nm Laser energy), Q-switched Ruby Laser phacopuncture; Nd: YAG laser phacopuncture, Nd: YAG laser anterior capsulotomy, Laser Induced Mechanical disruption using Nd: YAG 1064-nm laser energy are still in evolution. Though laser cataract surgery has shown much promise, but before it comes into wider acceptance, further research has to be undertaken.

1. ***Anaesthesia*** - Local Anaesthesia
   Topical/Intracameral/Peribulbar.
   General Anaesthesia
2. ***Incision Structure:***
   The key to SICS lies in the self sealing sutureless incision. Induced Astigmatism is directly proportional to the incision length and inversely proportional to the distance between the incision and the limbus[4]. The incisions are varied from circumlimbal (smile incision), straight to frown (chevran) shaped. The latter being preferred as it confines itself to within the astigmatic neutral zone.[4]
   a. ***Scleral tunnerl incision:*** It involves making a triplanar sealing incision. A scleral incision 0.3 mm deep, 1 mm behind the limbus is made, dissection is carried out into the clear cornea. Entry into the AC is made at the anterior most end of the tunnel.
   b. ***Clear Corneal Incision:*** Useful in certain situations - Complications like 'Oarlock' & Hyphaema are avoided. A functional trabeculectomy bleb is left undisturbed.
   c. ***Limbal Incision:*** Corneal Incision causes greatest, limbal intermediate and scleral least astigmatism.
3. **Capsulorhexis:**
   An important step in SICS is the continuous curvilinear capsulorhexis (CCC). While SICS is possible with can opner or linear capsulotomy, CCC provides a smooth and strong capsular bag of controllable size and shape without the risk of peripheral extension towards the equator. It also allows the implanted lens to remain exactly within the capsular bag and implantation possible on the rhexis in case of PC rupture.
   Alternately Radio frequency endodiathermy probe may be used.
   Lasers are also being evaluated for use in capsulorhexis.
   Special techniques of CCC include:
   Minicapusulorhexis, Bimanual Capsulorhexis and posterior capsulorhexis
   CCC and staining: In advanced cataracts CCC is performed after staining the anterior capsule with dyes[5]
   Dyes used are:
   Flourescein 0.2%, Indocyanine Green 0.5%, Trypan Blue 0.1%.
   Techniques: Staining under an air bubble, Intracameral subscapsular injection, Intracameral supracapsular injection.
4. **Hydroprocedures:**
   a. Hydrodissection: It is the separation of cortex from epinucleus.
   b. Hydrodilineation / Hydrodelamination
   Hydrodemarcation: It is defined as the separation of epinucleus from endonucleus.

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Hydrosonics: It is the use of ultrasonically driven needles to accomplish Hydrodissection and Hydrodilineation, and is an alternative to Manual procedures.

5. **Nucleus Management:**

   a. Blumenthal Technique: This is the preferred form of Manual SICS. The principle of this technique is Hydrodyanamic Expression.

   b. Visco expression Technique: Viseoelastic material like Methylcellulose is used instead of BSS during maneuvers like capsulorhexis or Nucleus Delivery.

   c. Phacofracture: Pioneered by Kansas and Modified by Drews, employs the division of Nucleus, using device like Nucleotome which fractures the Nucleus which is then removed piece by piece[6].

   d. Phacosandwich: The nucleus is sandwiched between a lens loop and a spatula and removed[6].

   e. Nucleus division with Snare: Snare is manipulated around the nucleus and tightened which divides the Nucleus, the fragments are then removed.[6]

   f. Hybrid Technique: Its major use is for those surgeons converting to phacoemulsification as it allows gradual transition step by step towards phaco.[6]

6. **Cortex washout:**
   Carried out by simcoe cannula / ACM

7. **Implantation of IOL:**
   IOL is implanted under viscoelastic cover, may be foldable or rigid, single or multiple piece.

8. **Wound Closure:**
   The wound is self sealing and no sutures are usually required but if valvular action is not attained, closure of the wound with sutures should be done.

   Results similar to phacoemulsification can be achieved with Manual SICS although without much hype and hardsell. With SICS the quest for 'No Glasses' at the end of operation is becoming more of a reality.

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VISION 2020: THE GLOBAL INITIATIVE FOR RIGHT TO SIGHT

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Introduction:

'Vision 2020: The 'Right to Sight' is a global campaign with objective of eliminating avoidable blindness by the year 2020. The World Health Organization (W.H.O.) in collaboration with various international non-government and private organisations launched it world wide on Feb 18, 1999.

Rationale for a global initiative to Combat avoidable blindness

Despite half a century of efforts, commencing with organized trachoma control, activities, the global burden of blindness is growing largely because of the population growth and aging. For example the life expectancy at the birth for an Indian 20 years back was approximately 50 years but now this has increased to 63 years. It has been projected that in countries like India, but the elderly population is likely to double in the next two decades implying a significant increase in visual impairment and blindness based on current levels of service. Already the backlog of blindness is very high and more over the existing resource in terms of infrastructure, human resource, etc., are not enough to meet the eye care needs. The gap between eye care needs and services levels is on the increase day by day. If additional resources are not urgently mobilized and efforts are not made to curb this trend, by 2020 the global burden of blindness can double with the developing countries bearing the burnt.

According to WHO, about 80% of blindess is avoidable as it results either from conditions that could have been prevented or controlled by applying the available knowledge and interventions (e.g. trachoma and onchocerciasis) or it can be successfully treated with sight restored (e.g. cataract). Blindness has profound human and socio-economic consequences in all societies. The costs of low productivity, rehabilitation and education of the blind are a significant economic burden, particularly in developing countries. Hence a concerted global campaign that aims to combat the major causes of blindness and give everyone in the world, particularly the millions of poor people, the right to sight was required. The idea of VISION 2020 came from USA, from the Director of the American CBM member association. The idea was well accepted by the WHO and other aid organisations, which joined forces to support this worldwide campaign.

Some of the facts and challenges associated with the global initiatives are:

- There are 45 million blind people throughout the world and 135-million with low vision.
- 90% of all blind people live in developing countries.
- In India, at least 9 million people are blind, in China 6 and in Africa 7 million.
- 80% of blindness on the earth is preventable.
- People in the developing world are ten times more likely to become blind than people in industrialized countries.
- People in the developing world are ten times more likely to become blind than people in industrialized countries.
- The world over, every five seconds one person goes blind and a child goes blind every minute.
- Every year, at least 7 million people go blind.
- By the year 2020, a total of 100 million people are to be saved from going blind.
- Blindness costs the national economies and annual worldwide sum of around 25 billmion US dollars.

These statistics alone should be reason enough for such a global initiative. With "Vision 2020," the number of blind people will drop out to about 25 million in the year 2020 and with out the programme; it would rise to almost 80 million from the current 45 million blind people.

What does 'Vision 2020' stand for?

In the USA, 20/20 stands for optimum eye sight. At the same time, it also denotes the year 2020. The objective "Vision 2020" is that no one should be needlessly blind any longer by the year 2020.

How is it different from existing strategies?

Vision 2020 is an initiative with a common objective, which will allow people cutting across nations, to work in a focussed and coordinated manner to help raise global awareness about blindness and mobilise additional resource to prevent or treat avoidable blindness. Vision 2020 will further develop and strengthen the primary health/eye care approach to the problem of avoidable blindness. This will be done on the basis of the invaluable international and national experiences already gained through the on going national programmes. Finally, the initiative will seek broad

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regional alliances and eventually a global partnership for the eye health. These partnerships are indispensable in establishing world wide the fundamental right "Right to Sight" and thus save future generations from the tragedy of needless blindness.

Vision 2020 partners

Besides the WHO the founding members of Vision 2020 include CBM international, The International Agency for Prevention of Blindness; Helen Keller International, ORBIS International and Sight Savers International. Vision 2020 is also supported by various non-governmental organisations from around the world.

Strategies for implementing Vision 2020

1. ***Control and prevention of major blinding diseases and disorders:*** Cataract Trachoma, Onchocerciasis, Childhood Blindness, Refractive Errors and Low Vision have been identified as immediate priorities based on the burden of blindness they represent and the feasibility and affordability of interventions to prevent and treat them.
2. ***Traning of human resource:*** Adequately trained human resources are a key factor for achieving the goals of Vision 2020. Training will need to be provided to ophthalmologists, refractionists, and managers of national/ regional prevention of blindness programmes. In India the target is to have one ophthalmologist per 50,000 population from the ratio of 1 per 100,000.
3. ***Strengthening the existing eye care infrastructure:*** Under the vision 2020- the estimates of the current status of infrastructure and the global targets have been listed under four highly inter related dimensions as illustrated in the following table:

	Current Status	Vision 2020 Targets
Availability	50%	95%
Accessibility	40%	90%
Utilization	25%	90%
Coverage	25%	90%

In the global scenario it is clear that the current infrasturcture has to be significantly increased in terms of eye hospitals, beds, equipment, and manpower. While establishing new infrastructure the issue of accessibility and coverage can be addressed by the following factors:

- Location
- Range of service
- Barriers to access
- Utilisation

4. ***Use of appropriate and affordable technology:*** Rapid advances are being made in the field of ophthalmology in the diagnosis and treatment of eye diseases. The same is happening in the specific focus area of Vision 2020, which are cataract, trachoma, childhood blindness, refractive errors, and low vision. Here the challenge in "Technology" is not so much innovating but adapting the new development to the local economies in a cost-effective manner. Initiatives that aim at transfer of technology so that manufacturing of high quality equipment and consumables at low cost by developing countries will be supported and promoted by Vision 2020. So the whole challenge is really in technology management. The technology management has to have a comprehensive approach and the various elements in such an approach are listed as:
   - Making it affordable
   - Developing skills in using them
   - Infrastructure for new technologies
   - Community awareness

Mobilisation of resource: The very first step towards Vision 2020 will be a global campaign to raise awareness among people and government about societal implications of blindness as well to mobilise a strong long term political and professional commitment to eliminate avoidable blindness. In the next millennium the economies are likely to grow at a fairly rapid rate in the Asian countries. Regardless of the economic changes, it is likely that the government and the NGOs, spending in eye care is likely to reduce considerably due to competing health and developmental needs. The competing health needs will come from the elderly population, which is expected, to double in the next two decades. There will be sharp increase in life style related diseases such as diabetes, hypertension etc which will be brought about by changes in diet, physical work pattern, and literacy. All this will demand additional resources. Against this scenario, the patients will increasingly become the major source of revenue. This can be supplemented to some extent by local and national charaties, which will need to be more aggressively developed and cultivated. As the patients become the major source of revenue, there will be greater accountability as they will be more demanding and will want good value for their money. Several models of this are already emerging in countries like India, Nepal, and Pakistan in which all economic groups within the service population are served through a system of internal cross subsidy. In order to achieve this paradigm shift, the focus will need to shift to quality, patient satisfaction and patient centered systems.

How will it be implemented?

Vision 2020 will be implemented through four 5 year plans, the first one starting in 2000. The three subsequent phases of implementation will commence in 2005, 2010,

and 2015 respectively. During the on going preparatory period, priority is given to issues of advocacy, regional planning, and resource mobilisation. The choice of the countries where Vision 2020 will be implemented is to be regionally proritized on the bass of burden of blindness and of available resources. Much of the philosophy of Vision 2020 lies in the recognition that by working together we can achieve what was previously not possible for individual agencies.

Funding

Presently the international community spends about 80 million dollars each year on the prevention of blindness. This amount has to be at least doubled if the targets set by Vision 2020 are to be achieved. Vision 2020 will also encourage governments and the United Nation agencies to increase funding for programmes in specific areas.

Spread awareness and make 'Vision 2020: the Right to Sight' a universal achievable basic right for every one. Your active involvement today will help the people in 2020 AD to be with perfect vision - 20/20.

AICA LOOP - A RARE CAUSE OF TREATABLE UNILATERAL PULSATILE TINITUS

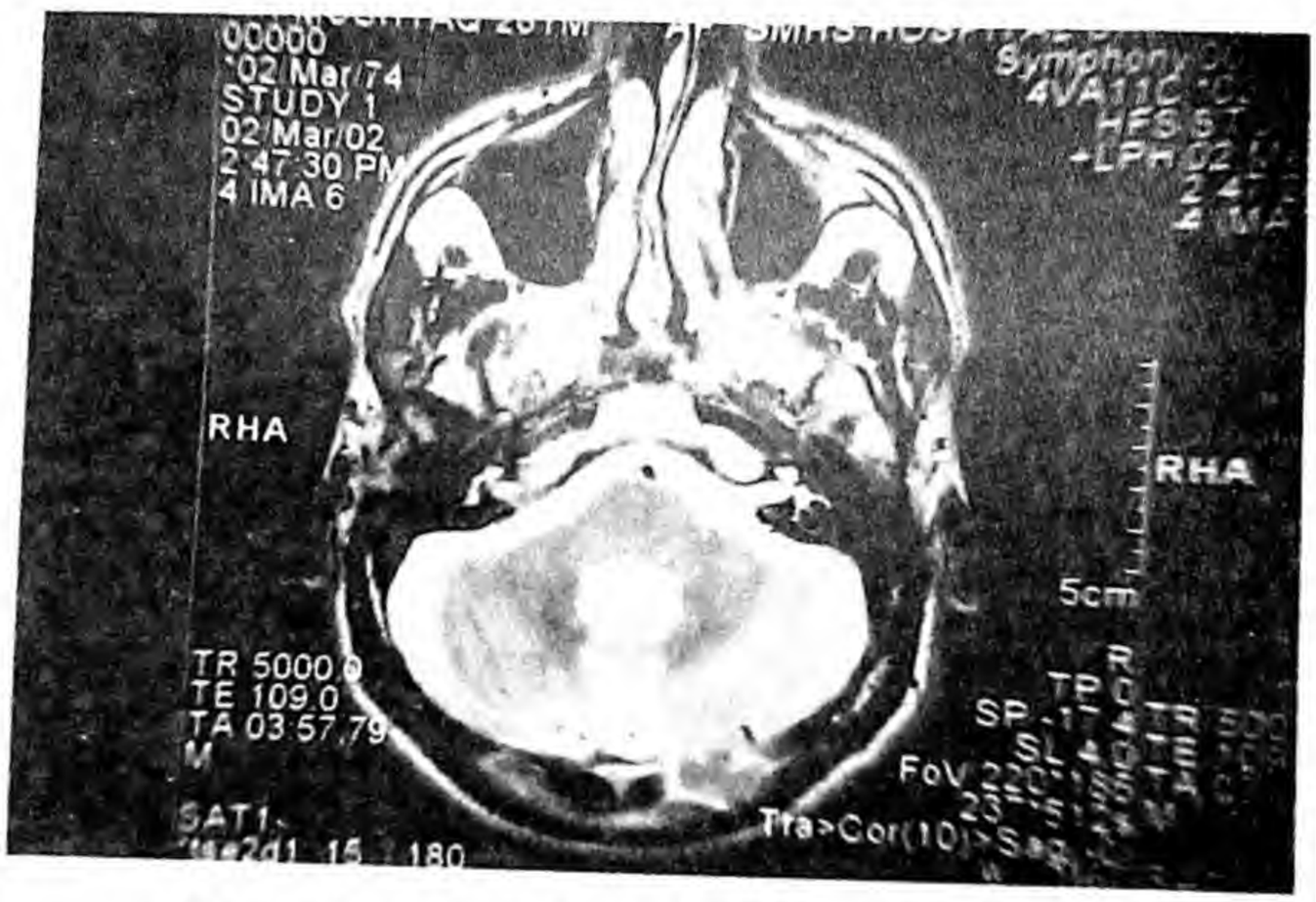

Fig-1: Normal 3D-TOF MR Angiogram.

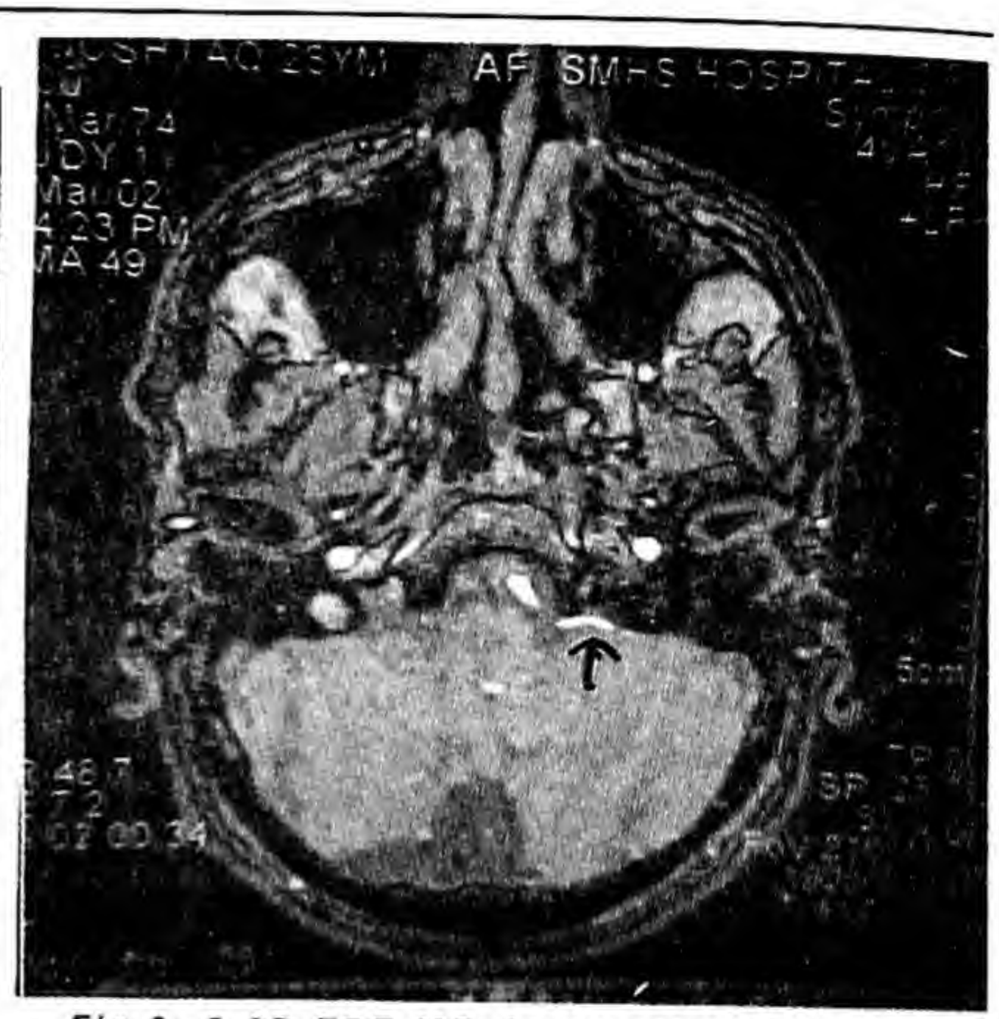

Fig-2: 2 3D-TOF MR Angiogramshows a loop of anterior inferior cerebellar artery (AICA) in the right internal auditory mcatus.

Pulsatile tinitus is seen in a variety of disordes like-aberrant ICA, dehiscent or high jugular bulb, AV malformation or fistula in temporal bone region, aneurysm in temporal bone region, high grade stenosis of ICA or ECA and paragangliomas.

Our patient, a 28 year old male medical student presented with pulsatile tinitus of right side. General physical and local ENT examination was unexplainable. Fundus was normal. On investigations, all biochemical parameters including serum calcium were normal His pure tone audiogram (PTA), impedance audiometery and CT scan ofthe temporal bone were normal. MRA was doen which showed a loop of AICA in the right internal auditory meatus. Loop is one of the rare causes of unilateral pulsatile tinitus which can be treated.

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THE HEALTH CONSEQUENCES OF ENVIRONMENTAL TOBACCO SMOKE

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This article was presented as a public awareness lecture by the first author on "Tobacco and Cancer" organised by the Cancer Society of Kashmir. Cigarette smoking is known to be the major single cause of preventable cancer deaths in the world today. It has been responsible for a steady increase in cancer mortality world wide especially in the United States over the past thirty-five years[1]. Environmental tobacco smoke (ETS) or passive smoke is the smoke inhaled by non-smokers from the environment. It is well known to have adverse health effects in non-smokers [2-4]. The intensity of exposure of passive smoke depends upon many factors namely the volume of air in the room, the number of active smokers, the rate of air exchange and the duration of exposure[5]. Exposure to ETS by non-smokers occurs frequently in homes,, in the workplaces and in other public areas where smoking is allowed. An infant or child of a smoking mother has the most intense exposure[5].

Components of environmental tobacco smoke:

Cigarette smoke is a complex mixture of over 4000 chemicals including 50 substances which act as carcinogens in animals or humans (Table I)[6-9]. The constituents also include cell irritants and toxins for example ammonia, formaldehyde and oxides of nitrogen; carbon monoxide and nicotine[5]. ETS consists of the following components:-

a) Mainstream smoke (MSS) the smoke inhaled and exhaled by the smoker, which constitutes 15% of ETS,
b) Side stream smoke (SSS) the smoke which comes out of the cigarette in between puffs, this is the most important constituent (85%) of passive smoke.
c) Vapour phase components that diffuse through the cigarette paper into the environment.

The constituents in MSS and SSS though similar in quality but vary quantitatively (Table II)[2]. The concentration of carbon monoxide is 2.5 times higher in SSS, thus making it more dangerous[10]. The particles in it are also smaller in diameter and can therefore reach the most distant alveolar portions of the lung[11]. Secondary chemical changes in the smoke also occur before a non-smoker inhales ETS[2]. Studies have shown that nicotine, its metabolite cotinine and carcinogens are detected in the blood, urine and saliva of non-smokers with passive smoke exposure[12-14]. ETS exposure occurs over an individual's entire lifetime.

Effect of environmental tobacco smoke on children and infants:

Infants are at a particular risk for damage from passive smoking because of the potential impairment of their developing organ systems especially the respiratory tract. Increased cotinine levels have been found in the saliva and urine of infants with household exposure to ETS[13,15]. A number of studies have demonstrated increased incidence of respiratory illnesses and hospitalizations in infants whose parents smoke[16-18]. There is significant correlation between infant hospitalizations for bronchitis and pneumonia from infants of smoking and non-smoking mothers ($P<0.001$) as shown in a study from Israel[17] with increase in hospital admission rates as per the number of cigarettes smoked by the mother per day. Similar findings have been reported in a study from the UK with further increase in illness if both parents smoked, this finding was independent of family size, socio-economic status and birth weight[16].

Children are already passively smoking on a regular basis by breathing the SSS from cigarettes lit and inhaled by their parents. They are also exposed to smoke in other environments such as schools and childcare settings. Such children show more restricted activity and bed disability days than children of non-smokers do. Furthermore the number of sick days is related to the number of cigarettes smoked by the patients[10]. These children suffer from persistent cough, bronchitis and middle ear infections[20-21]. Parental smoking is also a risk factor for childhood asthma, because the constituents of tobacco smoke are more likely to reach small airways; this is particularly true for SSS[22]. Thus children exposed to ETS experience an increase in respiratory infections and a decrease in lung function growth.

Acute irritating effects of ETS in adults are many. Many people have intolerance to tobacco smoke. People exposed to tobacco smoke develop conjunctival and nasal irritation, headaches and cough[23]. Even smokers are themselves annoyed by ETS causing disturbance in their work. 25%

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smokers and 50% of non-smokers experience eye irritation when exposed to smoke in their office[24]. The odour of ETS is also unpleasant for many individuals. This is principally related to the vapour phase. It is resistant to filtration systems but can be removed by ventilation systems.

Table-I: Carcinogens in Tobacco Smoke

1. Polyaromatic hydrocarbons:
   - Benzanthracene
   - Benzfluoranthene
2. N-Nitrosamines:
   - N-nitrosodimethylamine
   - N-nitrosoethyl methy lamine
3. Aromatic amines:
   - 2 naphthylamine
   - 2 toluidene
4. Inorganic compounds:
   - Arsenic
   - Chromiun
   - Lead
5. Aldehydes:
   - Acetaldehyde
   - For maldehyde
6. Other organic compounds:
   - Benzene
   - Vinylchloride

ETS and Lung Cancer in Adults:

That tobacco smoke causes lung cancer is well established and there are clear epidemiologic data for the same[25]. A number of studies have linked passive smoking with lung cancer[26-28]. Passive smoke contains carcinogens and there is no established lower threshold level of exposure for developing lung cancer. On the basis of these studies the Surgeon General of USA concluded that ETS causes lung cancer in non-smokers[29]. The risk is about 30% higher for non-smoking spouses of smokers than non-smoking spouses of non-smokers. The likelihood of lung cancer deaths among non-smoking wives of smokers was found to be 1.8 times that of non-smoking wives of non-smokers in a study from Japan[30]. The death rate also increased in direct proportion to the number of cigarettes smoked per day by the husbands. Other studies have also shown that both male and female non-smoking spouses had an increased risk of lung cancer if their spouses smoked[28,31].

Table-II: Constituents of Cigarette Smoke and the Ratio of SSS to MSS*

Gas Phase:		
Carbone monoxide	10-20mg	2.5 times
Carbon dioxide	20-60 mg	8.1
Methane	1.3 mg	3.1
Ammonia	80ug	73
AHydrogen cyanide	430 ug	0.25
Dimethyl nitrosamine	10-65 ug	52
Particular Phase:		
Tar	1-40 mg	1.7
Nicotine	1-2.5 mg	2.7
Toluene	108 ug	5.6
Phenol	20-150 ug	2.6
Benzpyreme	20-40 ug	2.8

** From Committee on passive smoking of the National Research Council 1986[2]*

ETS and cardiorespiratory disease:

The relationship of tobacco smoking to cardiovascular disease is well established and unequivocal[32,33]. Glantz and Parmley have shown the relationship between ETS and the risk of heart disease deaths in non-smoking spouses by analysing the results of ten epidemiologic studies[31]. The pooled relative risk for heart disease in non-smoking people of both sexes exposed to ETS from their spouses was 1.3. Evidence indicates that non-smokers are more sensitive to smoke[34] and SSS contains a higher concentration of gas constituents including carbon monoxide[10, 35].

Passive smoking is also associated with acute cardiovascular effects like hypertension, bradycardia and peripheral vasoconstriction besides worsening of angina pectoris. This peripheral vasoconstriction is more pronounced when SSS is compared with MSS[36]. Patients with angina pectoris exposed to cigarette smoke have tachycardia, increase in blood pressure, carboxyhemoglobin and carbon monoxide until angina develops and then a decrease is seen in the heart rate and blood pressure which can adversely affect oxygen delivery to the myocardium[37,38]. Physiologic and biochemical studies of acute and chronic ETS exposure show changes of endothelium, platelets, cellular respiration and exercise capacity from passive smoking similar to those of persons exposed to active smoking.

ETS also increases platelet aggregation and the nicotine directly damages the arterial endothelium. Platelets of non-smokers are also more sensitive to ETS,exposure than platelets of smokers[34]. About 37,000 deaths from coronary heart disease are attributed to passive smoking each year accounting for 70% of all deaths due to ETS[34]. Thus passive smoking is an important risk factor for heart disease mortality and morbidity. Some studies have shown a decrease in lung function tests in non-smokers exposed to ETS[30,39]. However, the clinical significance of these small changes in pulmonary fucntion in adults is uncertain.

Regulation of ETS legislation and private initiatives:

Keeping in mind the hazards of passive smoking, policies and legislation that restrict smoking in public places and the workplace should be adopted. Smoking restriction should be made a normal behaviour in society. Public awareness and acceptance of health risks of tobacco smoke

should be encouraged. The combination of altered social norms and opportunities to smoke may encourage smokers to quit and non-smokers especially teenagers not to start smoking. Over the past two decades, there has been a wave of social actions restricting or banning smoking in public places. This is the result of mounting scientific evidence about the health risks of involuntary tobacco smoke exposure and growing public antismoking sentiment[40]. Although the government has taken some action, for example the legislation banning smoking on all domestic airline flights and in some public places, the majority of the actions should be taken at the state and local level. These laws though likely to restrict smoking in the worksites will have the greatest effect on smoking behaviour and attitudes. They will also offer the greatest protection from passive smoking exposure[10]. Parents also have a role to play; they must be enlightened as to the consequences of parental smoking on children, the dangers resulting from exposure to ETS and the increased likelihood of smoking initiation among children of smokers.

Advocacy in the hospital-making it smoke free:

Health care facilities should be made smoke free. Firstly, smoking cessation is an integral part of the prevention and treatment of smoking-related diseases. A smoke-free environment should be an essential component of health care. Secondly, ETS can aggrevate the symptoms of respiratory and other diseases. Thirdly, employees should be protected from ETS exposure in hospitals; the doctors and para-medical staff should quit smoking. Finally, smoking is also a cause of hospital fires; hence hospitals should be made tobacco smoke-free.

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Workshop on Medical Informatics and Biomedical Communication sponsored by the Department of Biotechnology, JP Tropical Disease Research Centre (JBTDRC), Mahatma Gandhi Institute of Medical Sciences, 23 to 25 September at Sevagram (wardha). Contact Dr. B.C. Harinath, Co-ordinator, Bioinformatics Centre, JBTDRC, mahatma Gandhi Institute of Medical Sciences, Sevagram 442 102. Tel/Fax: 07152-84038. Email: jbtdrc@nagpur.doct.net.in

International Symposium on Bone Tumors, 26 to 28 September at New Delhi. Contact: Dr. S. rastogi, Tel: 011-659 3561, 659 3220, 659 3341 Fax: 011-6862663, 6521041, Email: rustogi@hotmail.com

13th Annual Conference of the Indian Society of Organ Transplantation, 27 to 30 September at Lucknow. pre-conference workshop on laparoscopic liver donor nephrectomy, 26 and 27 September. Contact the organising Secretary, Dr. Anant Kumar, Department of Urology and Renal Rmasplantation, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Raebareli Road, Lucknow 226 014. Tel: 0522-440 700,440 800, Ext: 2112, 2133, 2131 (O): 391 862, 398 456 (R): Fax: 440 017, 440 973; Email: anant@sgpgi.ac.in

XXXIII Annual Conference of the Indian Society of Nephrology, 15 to 17 Noember at Jaipur. For details contact the Organising Secretary, Dr. S.K. Pareek, E-1 Doctor's Enclave, Gangwal Park, Jaipur 302 004. Tel: 0141-618000, 602 525 (R), 560 291 - ext. 561 (H): Email: isncon 2002@datainfosys.net.

NAPCON-2002- 4th National Conference on Pulmonary Diseases under the auspices of the National College of Chest Physicians (India) and the India Chest Society, 20 to 24 Noember at Jaipur. For details contact the Organising Sectary, Dr. Nirmal Kumar Jain, A-123, Subhash Nagar Shopping Centre, Jaipur 302 016. Tel: 0141-304 348 (R), 304 414, 304 415 (H): email: napcon@indiatimes.com.

BIOLOGICAL MARKERS AND COLORECTAL CANCER

The prevalence of colon cancer is very high in the Western countries and colon cancer is the second leading cause of death from cancer in the United States (1). Colorectal carcinoma accounts for 98% of malignant tumors of the bowel and affects men and women equally[2]. Most of the colorectal tumors (90- 95%) arise from sporadic adenomas (polyps) and most of the remaining are accounted for by several hereditary cancer syndromes[2]. Despite advances in understanding the biology and natural history of colorectal cancer survival has not significantly improved in recent years. Fewer therapies are effective apart from timely surgery[2]. A polyp is defined as a mass that protrudes into the lumen of the colon. Polyps may be non-neoplastic or neoplastic. The non-neoplastic polyps are hyperplastic, inflammatory, juvenile or hamartomatous and lack dyplastic features. Adenomatous polyps are benign neoplasms that, by definition, display some dysplasia. Adenomatous polyps are widely believed to be the precursors of most of the colorectal adenocarcinomas and this concept is supported by epidemiological, genetic and pathological studies[2-8]. Patients with adenomatous polyps have a threefold higher risk of colon cancer over the general population and the risk increases to sixfold if the polyps are multiple[9]. The evolution of a carcinoma from an adenoma is generally believed to be a multi-step process of tumorigenesis called the, "adenoma- carcinoma sequence". This concept, postulated in the mid-seventies[7] is now widely accepted and has been supported by molecular genetics studies[10-16]. At the molecular level the initiating events in the tumorigenesis are a series of genetic alterations that confer a growth advantage to some cells over their progenitors leading to clonal expansion of these abnormal cells. These alterations may be mutations in the oncogenes like the K-ras gene or a tumor suppressor gene like the APC, P53 and DCC genes. Although only two mutations may be required to initiate the neoplastic process[2], Vogelstein and associates have suggested that malignant transformation may occur after accumulation of at least five major genetic faults[8]. The initial mutations in most of the cases occur at the APC tumor-suppresser gene locus (5 q21- q22)[2]. The initiated polyp may be present and proliferate for 10-15 years before undergoing malignant transformation[2,17].

The normal gastrointestinal epithelium is characterized by rapid cell turnover at the level of the colonic crypt, replacing the surface epithelium approximately every six days. The highly proliferative compartment is the lower third of the crypt. As the cells move up the crypt ,they mature, differentiate, lose their dividing ability and eventually die (apoptosis).

In the adenoma this orderly process is dysregulated. The proliferative compartment moves up to the surface of the crypt and there is continued mitosis, retarded cell maturation and differentiation and lack of cell death. The proliferative compartment finally takes over the entire crypt. At the histopathological level the earliest and the smallest recognizable entity may be an , " aberrant crypt focus (ACF)"[16]. Two types of ACFs have been observed in humans. The common one is a hypercellular crypt which has normal individual cells and is called the hyperplastic or non-dysplastic crypt because it is unlikely to lead to clinically significant lesions. Less common but more important are dysplastic ACFs which are believed to be the precursors of the adenomas and carcinomas and are referred to as unicryptal polyps[17-19]. The process of cellular proliferation is regulated by a number of regulatory proteins like oncoproteins, tumor suppresser gene products and cyclins[8]. Other growth factors like the epidermal growth factor, transforming growth factor-a, gastrin and enteroglucagon may also influence the proliferative activity of the gastrointestinal epithelium and play a role in colorectal carcinogenesis[20-21].

Various techniques have been used to study the proliferative activity in the colonic mucosa. Immunocytochemical methods are readily available and not as cumbersome as methods using Bromodeoxyuridine incorporation and autoradiographic studies using tritiated thymidine[22]. Proliferating cell nuclear antigen (PCNA) and Ki-67 are proliferation associated antigens mainly expressed in proliferating cells. They have been found to be very useful in studying the aforementioned abnormalities of the colonic crypt[22- 25].

The P53 gene is a tumor suppresser gene that appears to be the most important determinant of malignancy in colorectal neoplasia. It is located on the short arm of chromosome 17 and is frequently lost in colorectal malignancy. It is considered to be a transcription factor because it activates other genes and promotes their expression. These genes are involved in growth inhibition and loss of the P53 gene may therefore lead to unregulated cellular growth[26]. Mutations of P53 are found in more than 50% of all human cancers and more than 75% of colorectal adenocarcinomas, making it one of the most important

factors in human carcinogenesis[8, 27]. The varied functions of P53 including control of the cell cycle, DNA repair and programmed cell death have earned it the name, "guardian of the genome". Mutant P53 protein has a half-life of approximately 24 hours compared to wild-type P53 protein which has a half-life of 20 minutes. This extended half-life of mutant P53 (with lack of normal P53) allows it to accumulate and be over-expressed in tumors. The gene protein can then be easily recognized by immunohistochemical methods[28].

Normal colonic epithelium is polyclonal having arisen from multiple stem cells[10]. Studies of clonal composition of colonic tumors have revealed that all these tumors are monoclonal in composition[29]. The morphological evidence of this clonal expansion has been studied by DNA ploidy analysis. Flowcytometry is a simple technique and allows rapid measurement of DNA content in a large number of cells. Several studies on the nuclear DNA content of colorectal tumors have suggested that DNA aneuploidy is an important marker for malignant transformation of these tumors and is related to poor prognosis[30-33].

There has been increasing interest in tumor associated antigens in the colonic effluent for early diagnosis of colorectal cancer[34-38]. Recently Tobi et al have described an Adenoma-associated-antigen defined by a monoclonal antibody designated Adnab-9[39]. This 87-k Da protein antigen is present in a subpopulation of cells within an adenomatous polyp[40]. The binding of antibody to this antigen in colonic effluent seems to correlate with the risk of colorectal cancer[40-41].

Morphological and histological characters are the most important features of a polyp that correlate with its malignant potential. It is generally believed that the likelihood of invasive carcinoma increases with increased size of a polyp[42,43]. Over 80% polyps found on colonoscopy are <1 cm in size and only 2-3% are larger than 3 cm.. Only 1% of small (<1 cm) polyps have invasive cancer as compared to 10-20% of those larger than 2 cm[45]. Large distal colonic polyps (>1 cm) are also associated with increased prevalence of synchronous proximal polyps with advanced pathology[46-47]. Several studies have demonstrated an increased risk of developing subsequent cancer in patients with larger than 1 cm polyps on initial examination[9,47-48].

Neoplastic polyps are histologically divided into tubular adenomas, villous adenomas and mixed or tubulo-villous adenomas. The National Polyp Study reported that 87% of 3358 adenomatous polyps were tubular, 5 % villous and 8% tubulo-villous[49]. The risk of malignant transformation is low in tubular adenomas (2-3%) and high in pure villous adenomas (15-25%). The tubulo-villous adenomas have an intermediate risk of malignant transformation[45].

Many studies have demonstrated that having multiple polyps at the time of initial diagnosis increases the risk of developing subsequent adenomas and adenocarcinomas[48,50].

A polyp is called pedunculated when it has a stalk. One of the definitions is that a polyp is pedunculated if the length of the stalk is greater than its diameter[51]. In a review of literature, Coverlizza et al found that sessile polyps are more likely to have unfavorable histological features than pedunculated polyps[52].

By definition all colorectal adenomas are dysplastic. The degree of dysplasia has been graded into mild, moderate and severe on the basis of cytological and architectural features. The degree of dysplasia has been associated with malignant transformation. About 90% of patients with carcinoma have high grade dysplasia in the resected specimens and some authors believe that 40% of resected polyps with high grade dysplasia have a focus of "carcinoma in situ"[53]. To avoid confusion adenomas with severe dysplasia or "carcinoma in situ" have been called polyps with, "high grade dysplasia". It has been suggested that both "carcinoma in situ" and intramucosal carcinoma be reported as non-invasive carcinoma[54]. The predominant opinion among gastrointestinal pathologists is that the spread of neoplastic cells through the muscularis mucosae should be considered to be an invasive carcinoma[54-55]. A polyp with invasive carcinoma is also called a "malignant polyp".

Complete endoscopic removal of an adenoma with a non-invasive carcinoma represents a cure. Although most of the polyps with invasive carcinoma are adequately treated by endoscopic polypectomy, about 10% patients will have residual cancer in the colonic wall or lymph nodes at the time of polypectomy or on follow-up[52,54,56]. Prognostic criteria have therefore been formulated to help in the proper management of these patients[52,54,56]. Prognostically favorabie features include complete endoscopic resection, well differentiated histology, clear margin of resection and lack of vascular and/ or lymphatic invasion[52,54,56].

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SEXUAL BEHAVIOURAL CHANGES FOR HIV: KEY APPROACHES

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INTRODUCTION

Nowadays, interventions to stem the spread of the human immunodeficiency virus(HIV) throughout the world are as varied as the contexts in which we find them.Not only is the HIV epidemic dynamic in terms of treatment options,prevention strategies and disease progression, but sexual behaviour which remains the primary target of AIDS prevention efforts worldwide, is widely diverse and deeply embedded in individual desires, social and cultural relationships, and environmental and economic processes.This makes prevention of HIV, which could be an essentially simple task, enormously complex involving a multiplicity of dimensions.

Either implicitly or explicitly nearly all prevention interventions are based on theory . Most rely on the assumption that giving correct information about transmission and prevention will lead to behavioural change. Yet research has proved numerous times that education alone is not sufficient to induce behavioural change among most individuals. Thus, second – generation interventions have been developed based on individual psychosocial and cognitive approaches that educate individuals in practical skills to reduce their risk for HIV infection.[1,2] More recently, social researchers have come to realize that because complex health behaviors such as sex takes place in context, socio-cultural factors surrounding the individual must be considered in designing prevention interventions.Finally, beyond the individual and his or her immediate social relationships lie the larger issues of structural and environmental determinants that also play a significant role in sexual behaviour.[3]

The most common approaches used to influence HIV risk reduction are:

A) APPROACHES AIMED AT INDIVIDUAL LEVEL BEHAVIOURAL CHANGE

1) INFORMATION, EDUCATION AND COMMUNICATION

Mass and small group education

As information was initially , for many, thought to be the key to behavioural change, HIV prevention programmes began with a focus on increasing awareness about the modes of transmission and prevention.[4]Mass education for HIV prevention can take many forms but is often seen as a key component of a comphrehensive AIDS prevention programme.[5] Mass media, for example, are directed to the general public and aim at teaching people essential facts, promoting healthy behavior, quieting anxiety about casual transmission and preventing discrimination.

Small group AIDS education is taking place all over the world, advancing general knowledge of HIV in numerous communities. Small group AIDS prevention programmes can be seen as having three main components: content,context and strategies. Content includes goals, objectives and activities.The main content areas in most small- group intervention activities include: basic education about AIDS, sensitization to one's personal risks for HIV, instruction in individual actions that can reduce one's risk and exploring new ways to communication with sex partners. Entire interventions or research questions are built on any one of these content areas.

The second component in small group HIV prevention is the context.The different aspects of the intervention should be designed to fit the cultural, gender and developmental issues of participants.The third component,strategy is the process itself, where emphasis is placed on how the interventions are implemented between participants and group leader.Key elements to consider include how to foster trust, build group cohesiveness, encourage motivation and mutual support among participants and the facilitator.[6]

Although evaluations of small- group interventions have focused on content and facilitation skills, all three components have been found to be critical to the success of this approach.

Peer education

Peer education is one approach to small-group HIV

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prevention usually aimed at individual behaviour. The peer health educator approach recruits leaders in communities at risk to be implementers of the education programme to their peers. Selection of peer educators is a key to the success of a programme and often involves:

- Acceptance by other members of the group
- Being an opinion leader,thus well respected in the group
- Willingness to be trained
- Committed to the goals of the programme.

Many interventions combine peer education with other approaches such as the use of social networks, condom social-marketing and outreach as these approaches can be complimentary.[7,8] Outreach work using peers has resulted in increased diversity of participants.[9]The benefits of working with peers rather than with 'experts' from outside the social network are many depending upon the group at risk. Peer educators maybe a more credible source of information for women, may communicate in a more understandable language and serve as positive role models.[10]

2) TESTING AND COUNSELLING

In increasing numbers, people in industrialized countries are receiving their HIV test results as therapeutic options become available to more people. Early detection of the virus enables referral for clinical care and psychosocial support.Ethically people have a right to know their serostatus in order to protect themselves and others.And knowing their own serostatus and the options can motivate people to change high risk behaviours. The theoretical foundation on which interventions providing testing and counselling are built principally involves the stages of change model. HIV testing and counselling may promote progression across the continuum of the stages of change. For example, in rural southwestern Uganda, a setting with high HIV prevalence, the majority of respondents in a research study reported that they had already made behavioural changes because of AIDS, but making further changes to protect themselves was contingent on knowing their HIV serostatus. It has thus been suggested that counselling promotes risk reduction through increased perception of risk, self-efficacy and personal skills and through reinforcing social norms or responsibility.[11]

B) APPROACHES AIMED AT THE COMMUNITY-LEVEL

Community- level approaches have grown out of the realization that, despite the considerable risk reduction through individual- level behavioural change approaches, different approaches are needed as well. Social epidemiology, pointing to differences in prevalence among different social categories within a given risk category in a community suggested interventions along those lines.[12]

Community- level interventions include:

1) SOCIAL INFLUENCE AND SOCIAL NETWORK INTERVENTIONS

Based on the theories of social influence, diffusion of innovation, reasoned action and social cognitive theory, these interventions use peers and social networks to disseminate information. Social influence interventions identify key persons in communities who are capable of influencing others. Research implemented using peer educators to influence social networks in gay communities showed significant self-reported changes in safer sex practices after intervention.[13]Encouraging results in changing social norms and safer sex behaviour have also been noted in a number of community-level social influence interventions in the USA.

2) OUTREACH INTERVENTIONS

Outreach interventions are conceptualized in a similar manner to social influence interventions in that they use individuals to pass on information within social networks, however the influential person may or maynot be from the targeted community. The outreach worker enters the social system to instigate behavioural change as an individual change agent.Targeted communities are often hard- to-reach groups such as drug users, sex partners of drug users, sexworkers as well as isolated rural populations.The aims of outreach have often been harm reduction strategies such as providing condoms to sexworkers but not necessarily addressing sexwork itself.

3). SCHOOL-BASED INTERVENTIONS

By the early 1990s , school-based programmes for HIV education existed in about three quarters of industrialized countries and 60% of developing countries according to a survey of 38 countries.[4]Besides interventions that simply provide basic AIDS information in the classroom, multi-dimensional school-based programmes generally include classroom skills-building sessions, school-wide peer-led activities, and social norm changing programmes. Promotion of condom use was the theme most frequently adopted in programmes for youth in and out of school. The element distinguishing school-based programmes from other interventions for youth was the supportive structural aspect played by schools and teachers, and the interaction between school, parents, students and community.[6,14]

3) CONDOM PROMOTION AND SOCIAL MARKETING

It has now been proven numerous times that correct use of condoms is aneffective method of preventing HIV transmission. Yet, countless research studies have identified obstacles to their use in settings throughout the world, including inaccessibility and partner communication among other factors. Most initial HIV prevention programmes included condom promotion and free distribution as part of a comprehensive HIV prevention package. Free distribution was essentially aimed at introducing condoms where they were not previously available or distributing them to destitute populations at high risk such as sexworkers and refugees. Although this approach accomplished its intended outcome of making condoms accessible without delay to large populations, the lack of sustainability and reliability of free condom distribution programmes commanded the introduction of condom social marketing strategies especially aimed at certain populations.Condom social marketing ,which may well be the most developed of public health communication approaches,aims to remove the barriers to condom use by using commercial marketing techniques such as advertising and packaging to make the product accessible, affordable and attractive to all types of people.Social marketing has been termed a 'strategic planning' approach based on the theoretical 'principle of exchange' which explains that people will only change their behaviour to something less pleasant(like condom use) if they perceive an adequate benefit. Making condoms available at non-traditional outlets such as truck stops,bars and hotels is integral to social marketing success.Flooding these non-traditional outlets with condoms aims not only to increase availability but also to increase social acceptability.[15]

4) COMMUNITY ORGANIZATION,EMPOWERMENT AND PARTICIPATORY ACTION RESEARCH.

Empowerment approaches are built on the premise that public health impact is fostered by recognizing the relationship between social structure and health, and by recognizing that lasting change is a process that initiates from within a community. Community participation at all levels of implementation is an integral aspect of community empowerment approaches.Interventions include community organizing and participatory action research (PAR) into their programmes. [16]A strength of PAR resides in the ability of participants in conjunction with committed and creative professionals to adapt methods and content to diverse contexts. The positive outcomes of PAR arise from its collaborative , trust-building capacity , with direct community input that responds to emerging changes in social, political and economic situations.[17,18] These interventions seek to support communities to be self-determining in their ability to integrate HIV programmes into existing community structures by assessing their own needs and priorities ,defining,implementing and evaluating their own work..

5) POLICY LEVEL INTERVENTIONS

Policy level interventions are 'enabling' approaches that attempt to remove structural barriers at a larger level.Many believe that AIDS interventions are moving from solely investigating individual approaches to multidimensional models of community mobilization, empowerment and structural policy level interventions .[19]A widely recognized policy level intervention is the 100% condom programme in Thailand that mandated condom use in brothels and during other commercial sex encounters.Components of the programme included a requirement that sexworkers use condoms with all clients ,that condom use be monitored, that brothel owners and managers assist in promoting condom use with uncooperative clients and that there should be sanctions against brothel owners for non-compliance.[20]The programme showed a dramatic increase in self-reported condom use during commercial sex acts(14% to 90%), a decline in reported STD attendees in government clinics, and a decline of HIV positive army conscipts.[12]Success of the programme has been attributed to the fact that it was based on harm reduction in a population at very high risk.It did not try to eliminate the brothels but attempted to reduce HIV transmission within them, and it used national policy which ensured a broad and lasting effort.

CONCLUSIONS

Safer sexual behaviour remains the single most effective method of preventing HIV infection. An important point stressed by focussing on behavioural change approaches is the need to see different levels of HIV prevention initiatives as complimentary. Individual approaches have shown impact, but to stem transmission on a larger scale for longer term maintenance of changed behaviour,community and structural level programmes are a critical compliment.These approaches, despite showing great potential, have not yet been operationalized on a large scale.At this stage programmes should emphasize trans-theoretical approaches that combine individual level constructs with community-level projects that focus on subcultural norm changing.Community organizing can have the powerful effect of imparting a unified sense of purpose and new beliefs in the possibility of change.Despite the many advances in the field and many changes in behaviour observed, populations at highest risk have not received their share of the attention and resources allocated to AIDS interventions globally.The countries with the highest prevalence of HIV are those with the least resources and

strained medical and social support systems.These countries with the highest prevalences of HIV are those with the least resources and strained medical and social support systems.These countries with rapidly changing epidemics do not have the means alone to develop randomized controlled trials to test behavioural interventions,yet they are the communities needing the interventions the most urgently.Most theory driven intervention research has been conducted in industrialized countries with very different epidemics to those in developing countries. It is therefore critical to test models and approaches across cultural, economic and social situations.In an epidemic where changes are occurring rapidly at the level of the virus, treatment context and within populations at risk multi-dimensional interventions based on theories and models which address individual as well as contextual and sociocultural variables such as gender, class and ethnicity ,and their influence on sexual behaviour are urgently needed.

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INTERCONDYLAR LOCKED DISLOCATION OF PATELLA WITH VERTICAL AXIS ROTATION: A SIMPLE METHOD OF CLOSED REDUCTION

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ABSTRACT: Intercondylar vertical dislocation of Patella is a very rare injury occurring usually when patella rotates around its vertical axis and gets locked in the intercondylar area. A simple method of closed reduction is described based on the peculiar anatomical configuration of distal patellar articular surface of the femoral condyles.

Key Words: Patella, Dislocation vertical

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INTRODUCTION:

Lateral dislocation is the most common type of dislocation of Patella. Intra-articular dislocation of patella is a rare injury, the most commonly reported is a horizontal type in which the patella rotates around its horizontal axis and gets locked with its articular surface facing superiorly or inferiorly[1-3]. Few cases of superior dislocation of patella have been reported in osteoarthritic knees with their inferior pole locking against osteophytes[4,5]. A vertical dislocation of patella is a very rare injury. The patella rotates around its vertical axis with the articular surface facing medially or laterally. To our knowledge only eight cases have so far been reported in the literature[6-12].

We report two cases of this unusual vertical dislocation of patella and a simple method of closed reduction based on the peculiar anatomical configuration of anterior patellar surface of femur.

MATERIAL AND METHODS:

The traumatic lateral dislocation of the patella is a well-described clinical entity and closed reduction is accomplished easily even in an emergency room. The other types of patellar dislocations, especially those involving patellar rotation around its vertical axis, are unusual. We have come across only eight cases of this type of injury in the literature and have studied the mode of injury and method of reduction adopted for each individual case. They have most often been associated with sports activities such as football or soccer, and occur mostly as a result of direct blow to the lateral or medial aspect of fully extended knee. The patella rotates around its vertical axis resulting in twisting of the patellar and quadriceps tendons with the patellar articular surface facing laterally or medially. In most of the cases reduction has been achieved by closed means under general anaesthesia. In three of the cases closed reduction has been unsuccessful and open methods were used to achieve reduction [1,4,7]. We have come across two such cases with an indirect mode of injury and have devised a simple method of closed reduction based on peculiar anatomical configuration of patellar articular surface of femur.

Case 1:

A 25-year-old healthy boy stumbled while walking when his big toe of right foot got stuck within the trousers of the opposite limb resulting in forced internal rotation of the right limb. The patient was brought to the hospital in severe pain with his right knee in full extension. Examination revealed vertical position of patella in front of the affected knee. There was tenting of the overlying intact skin. The distal neuro-vascular examination was normal. Roentgenogram of the knee demonstrated the medial border of the patella hitching over the intercondylar area of the femur (Fig. 1, 2). The quadriceps muscle being in spasm, several attempts at closed reduction without anaesthesia failed and produced more discomfort to the patient. The reduction was achieved under general anaesthesia. The inferio-lateral border of the patella was pushed in superio-medial direction with an outward rotating force to un-twist the twisted patellar and quadriceps tendons and the patella slipped back to its normal anatomical position. Check radiograph confirmed the reduction and no osteochondral fracture was seen. Further evaluation of the patient did not reveal any predisposing condition for dislocation. The knee was immobilised in a posterior slab for three weeks. Static quadriceps exercises were started immediately. After 6

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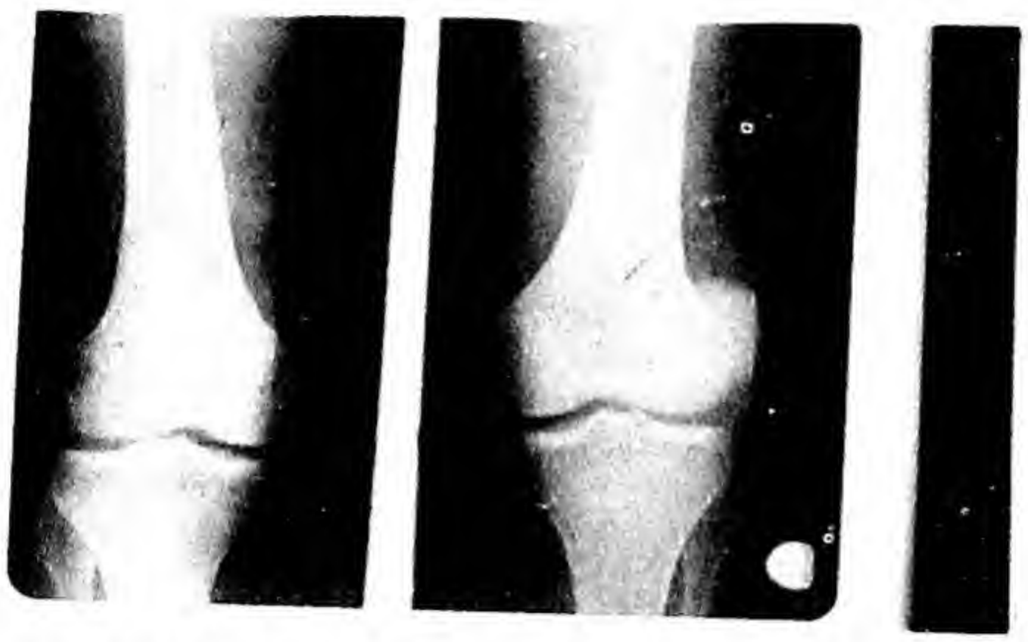


Fig. 1: X-ray anterio-posterior view of both knees showing vertical dislocation of patella on right side.

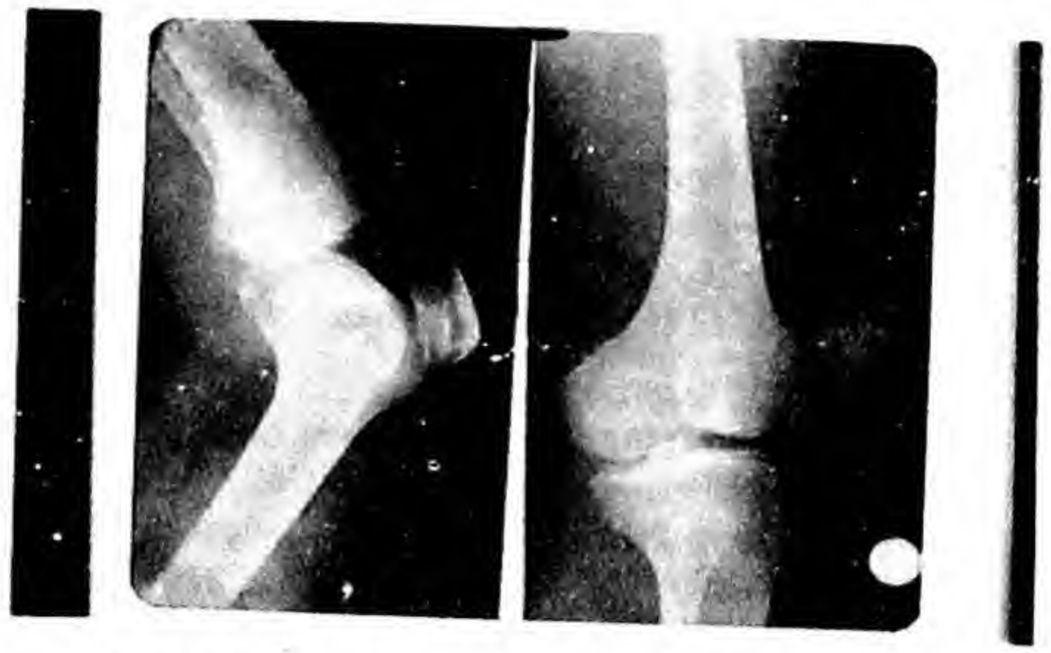


Fig. 2: X-ray lateral view of both knees showing vertical dislocation of patella on right side.

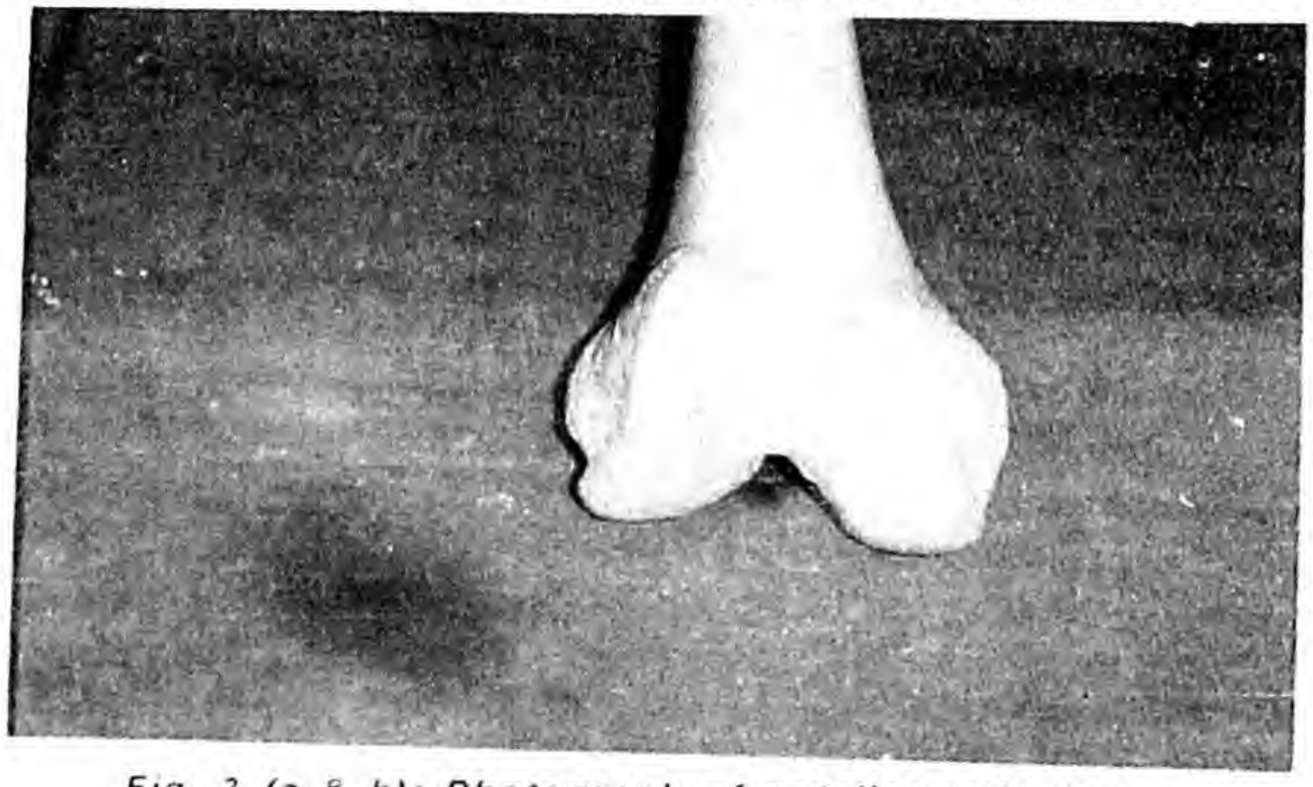


Fig. 3 (a & b): Photograph of patellar articular suface of normal femur showing lateral femoral condyle projected more anteriorly than the medical femoral condyle throughout its length but there is flattening of proximal portion of patellar articular surface of medical femoral condyle. This results in formation of a slope from lateral to medical side in the proximal position

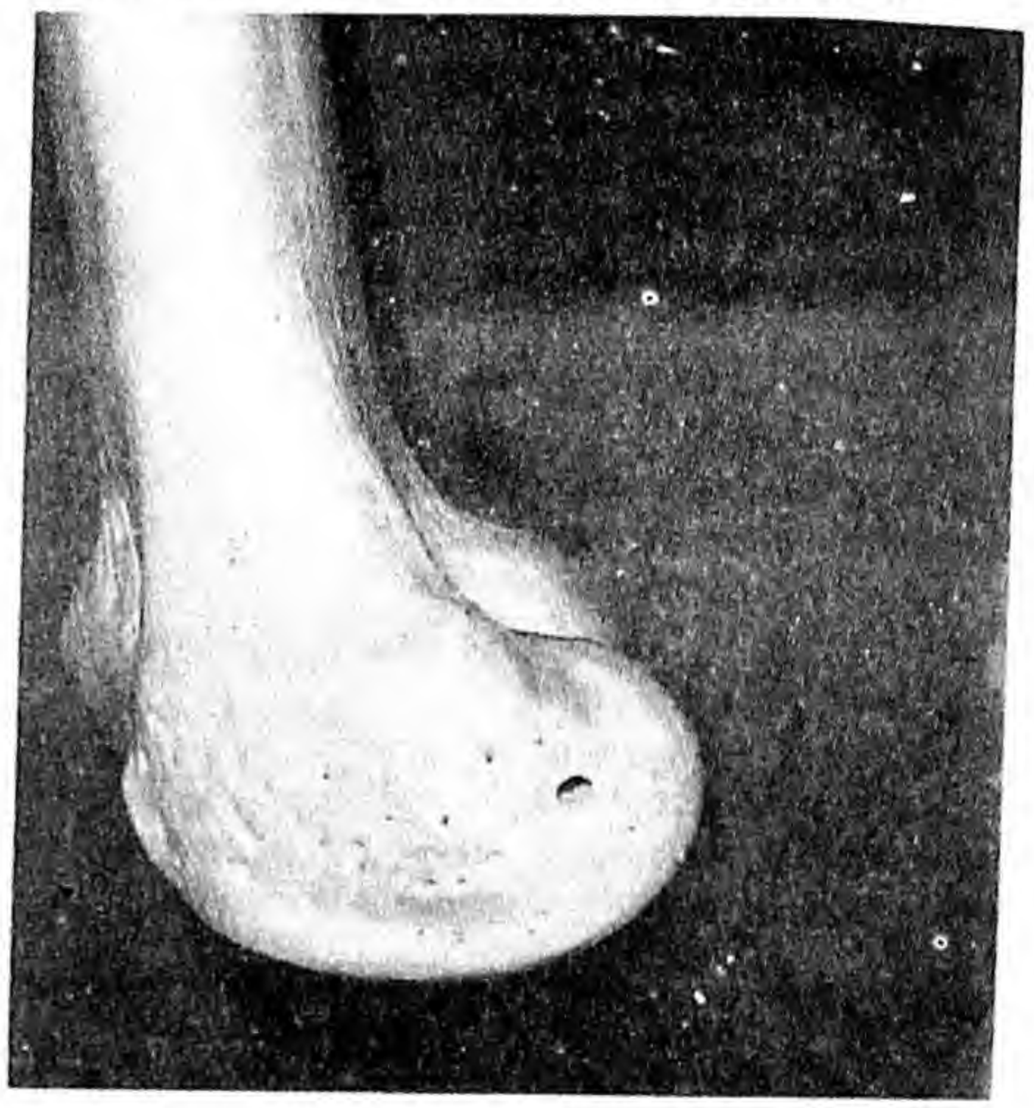
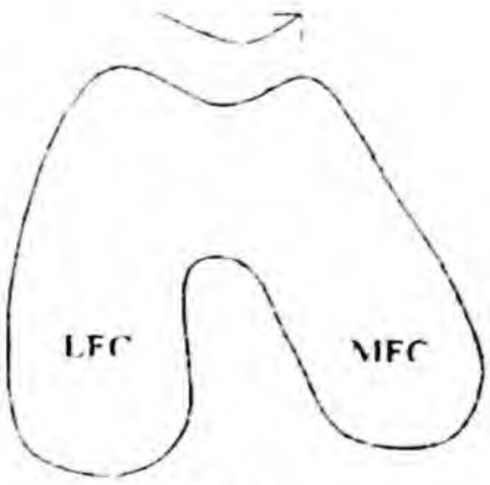
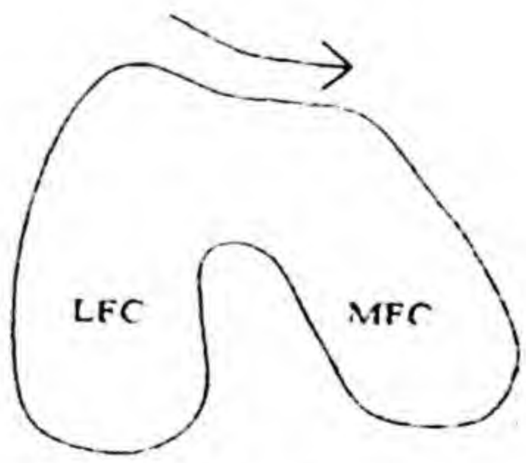


Fig. b:



[A]



[B]

Fig. 4 (A & B): Diagrammatic representation of cut section at the level of patellar articular surface of femur in the distal (A) and proximal (B) portion. The proximal portion forms a slope from lateral to medical patellar articular surface and thus helps in reduction of vertical dislocation once inferio-lateral pole of the patella is pushed in superio-medical direction with an outward rotating force.

weeks of reduction, the patient had achieved full range of motion of knee with minimal discomfort while climbing upstairs. There was no demonstrable ligamentous laxity. At one year follow up the patient had no discomfort, no patellar tenderness and apprehension test was negative.

Case 2:

A 35-year-old female sustained vertical dislocation of patella of her right knee. She was sitting with her both knees in a position short of full extension. She was carrying her baby in her hands when it suddenly slipped out of her hands on left side. In order to catch hold of the baby her right knee got hyper extended and the leg rotated internally. She experienced severe pain and noticed deformity of right knee. Clinical examination revealed the vertical position of patella, hyper extended knee and tenting of overlying skin. The distal neurovascular examination was normal. Roentgenogram of right knee confirmed the vertical position of patella with its articular surface facing laterally. The patient was anaesthetised and reduction achieved easily by pushing the inferio-lateral pole of patella in superio-medial direction with an outward rotating force. Check X-ray demonstrated normal position of patella with no osteochondral fracture. Again there was no predisposing condition for patellar dislocation. The knee was immobilised in a plaster of paris slab for three weeks. Full range of motion was achieved in 6 weeks. Patello-femoral pain and minimal effusion persisted for 8 weeks. At one year follow up the patient was asymptomatic with no ligamentous instability and the apprehension test was negative.

DISCUSSION

Several cases of intra-articular dislocation of patella have been reported in the literature with the patella rotating around its horizontal axis and getting locked under the femoral condyles and its articular surface facing superiorly or inferiorly[1-3]. Most of the dislocations occur with the articular surface facing inferiorly and the knee being held in slight flexion. ***Frangakis*** believed the mechanism to begin with direct trauma on the partially flexed knee. The upper pole is pushed posteriorly into the joint, which locks. The quadriceps muscle detaches from the upper pole of the patella. As the quadriceps muscle contracts, the moment of force produces the remaining rotation of the patella[7]. These dislocations are complicated by osteochondral fractures. Although closed reduction has been reported, the vast majority of horizontal dislocations require open reduction. No recurrence of dislocations has been reported.

In the vertical dislocation of patella the knee is held in full extension. The mechanism of injury in this type of dislocation has not been clearly defined. Mostly they have been associated with sports activity such as soccer and occur as a result of direct blow to the medial or lateral aspect of the fully extended knee[6,7,8,10,11]. ***Colville*** described the injury of a 16-year-old football player, which resulted when a tackler landed on the lateral side of the patient's extended leg. He suggested the mechanism was a severe valgus stress on the extended knee[3]. ***Levin*** reported a case of a 16-year-old patient who sustained a vertical dislocation of the patella while kicking a soccer ball. He theorised that injury occurred when the patient externally rotated the tibia with knee slightly flexed and then internally rotated the tibia and hyper extended the knee so rapidly that the patella could not glide back into its normal position[13].

The mechanism of injury in our case is almost the same as that theorised by ***Levin.*** The partially flexed knee and externally rotating tibia is suddenly internally rotated and hyper extended so rapidly that the patella cannot glide back into its normal position. The patella rotates around its vertical axis and gets locked with its medial border perching over the intercondylar area anteriorly. The tight quadriceps expansion acts like a bowstring and prevents the relocation of patella. As the forces are perpendicular to the longitudinal forces of the patella, there is no necessary injury to the patellar or quadriceps tendon in contradiction to the horizontal dislocation but some degree of disruption of the retinaculum occurs to allow rotation of the Patella[1]. Most of the vertical dislocations of the patella can be reduced by closed means. A knee immobilizer adequately immobilizes the soft tissues to bermit healing within 3-4 weels.To understand the method of closed reduction, it is necessary to know the anatomy of femoral condyles. The lateral femoral condyle is projected more anteriorly than the medial femoral condyle and in the proximal portion, the patellar articular surface of the medial femoral condyle flattens while as that of the lateral femoral condyle is still projected anteriorly making a slope towards the medial femoral condyle (Fig. 3,4). Thus it is easier to reduce the patellar dislocation from its vertical position in the intercondylar area of femur with the articular surface facing laterally, by pushing its inferio-lateral pole in superio-medial direction towards the flattened portion of medial femoral condyle with an outward rotating force. Pulling the patella distally to unlock it from the joint as advocated by **Alioto** and **Kates** in their method of open reduction with the help of Shanz screw inserted from the non-articular surface, seems more difficult because of persistence of intercondylar groove throughout the distal portion of the patellar articular surface of femur and the tight quadriceps expansion

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STEFFEE (VSP) INSTRUMENTATION FOR THE SURGICAL MANAGEMENT OF THORACOLUMBAR SPINAL FRACTURES. (A STUDY OF 20 CASES).

S. Afzal; M.R. Mir; M.A. Halwai; A. Shabir

Abstract: *Twenty patients are reported here. Fifteen patients had injury at thoracolumbar junction and five patietns had injury with unstable tohraco-lumbar and lumbar spine fractures treated with steffee[5] instrumentation done between the period November 2000 and January 200. at the department of Orthopaedic Syrgery, Govt. Medical College Srinagar at different leels of lumbar spine. There was an overall corrections of kyphosis post-operatively with some loss of kyphosis at follow-up from operative correction. One patient had backward migration of a screw. Two patients had wrong placement of pedicle screws. There was no implant failure in our study. One patient had complaints of consistent pain along the left lumbar region for which no organic cuase was found and was treated with anti-psychotics to which patient responded. One patient had developed Grade-I pressure sore which healed by treatment. 50% of our patients had neurologic deficit of of different grades of frankel. Average stay in hospital was 10 days. Patients were operated within seven days following trauma.*

Key words: *Thoraco-lumbar fracture, Lumbar fracture, VSP instrumentation, Steffee plates,pedicle screws.*

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The modern era of posterior spinal instrumentation for spinal fractures began when HARRINGTON(1958)[1] first used dual distraction rod for treatment of these injuries.

The history of vertebral screw fixation dates back when KING(1944)[2] first described the placement of screws parallel to inferior border of lamina and across the facet joints.

External transpedicular fixation of lower thoracic and lumbar spine was developed by MAGEREL in 1977.(fixator externae) [3].The foundation for pedicle screw and posterior plates was set by ROY-CAMILLE [4] in 1970.

STEFFEE [5] in 1982 developed a new segmental instrumentation of pedicle screws and variable spinal plates.The plates have long slots which can be fixed over the screws and have nests in which the special pedicle screws get locked and prevent the plate from moving.It can be used from lower thoracic spine to the sacrum.

Pedicle screw fixation has enabled the surgeons to instrument "one above and one below"(two motion segments) thus decreasing the exposure,preserving motion segments,avoiding long fusions,providing a stable construct.

Eduardo Luque(1986) [6],introduced another method of interpeduncular segmental fixation using pedicle screws wired to Luque rods.

MATERIALS AND METHODS:

Between November 2000 and December 2001 twenty(20) patients underwent stabilization and fusion using steffee instrumentation for unstable thoraco-lumbar and lumbar spinal injuries in our hospital.Follow up information was available for all the patients.There were 16 men and 4 women.Majority (80%) of our patients were men of low socio-economic status with history of fall from height in all of our patients while on there jobs.The average age at the time of surgery was 32 years(18-46 years).The average follow-up was 7.5months(3-12months).14 patients had injury at thoraco-lumbar level and 6 patients had injury at different levels of lumbar spine.The patients were discharged from hospital at an average of 10 days after surgery.10 patients had neurologic deficit of varying FRANKEL [7] grades.

All patients were admitted through the emergency department .All patients were evaluated thoroughly at the time of admission and looked for any other injuries .A complete neurologic examination was performed at the time of admission and presence or abscence of bulbo-cavernosus reflex was recorded.

Neurologic compromise was classified according to the system described by FRANKEL [7].Initial management in the form of i.v.fluids,analgesics and other medical treatment

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Figure 1.Post-op X-rays(ap/lat).#-Dislocation D11-D12.

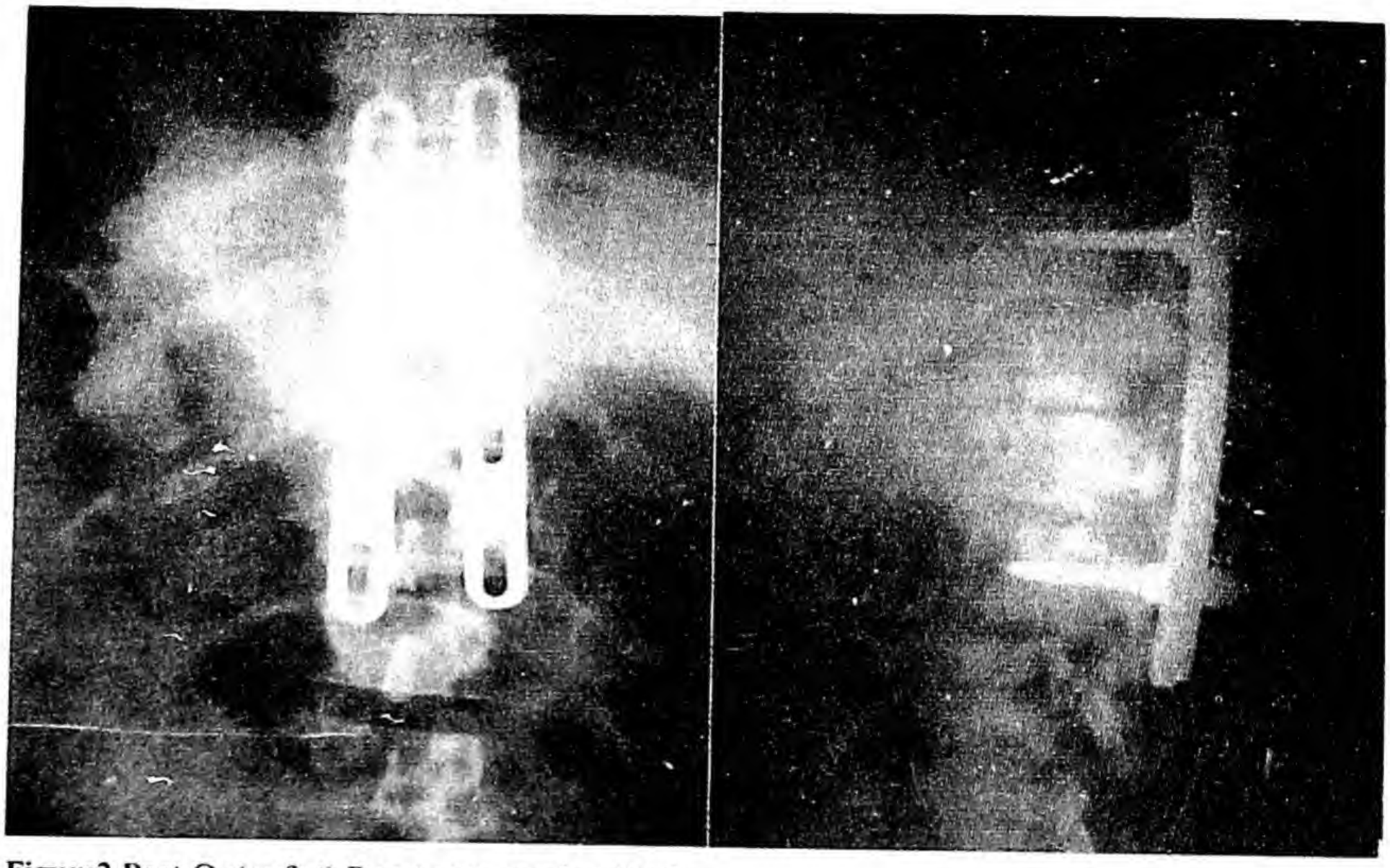
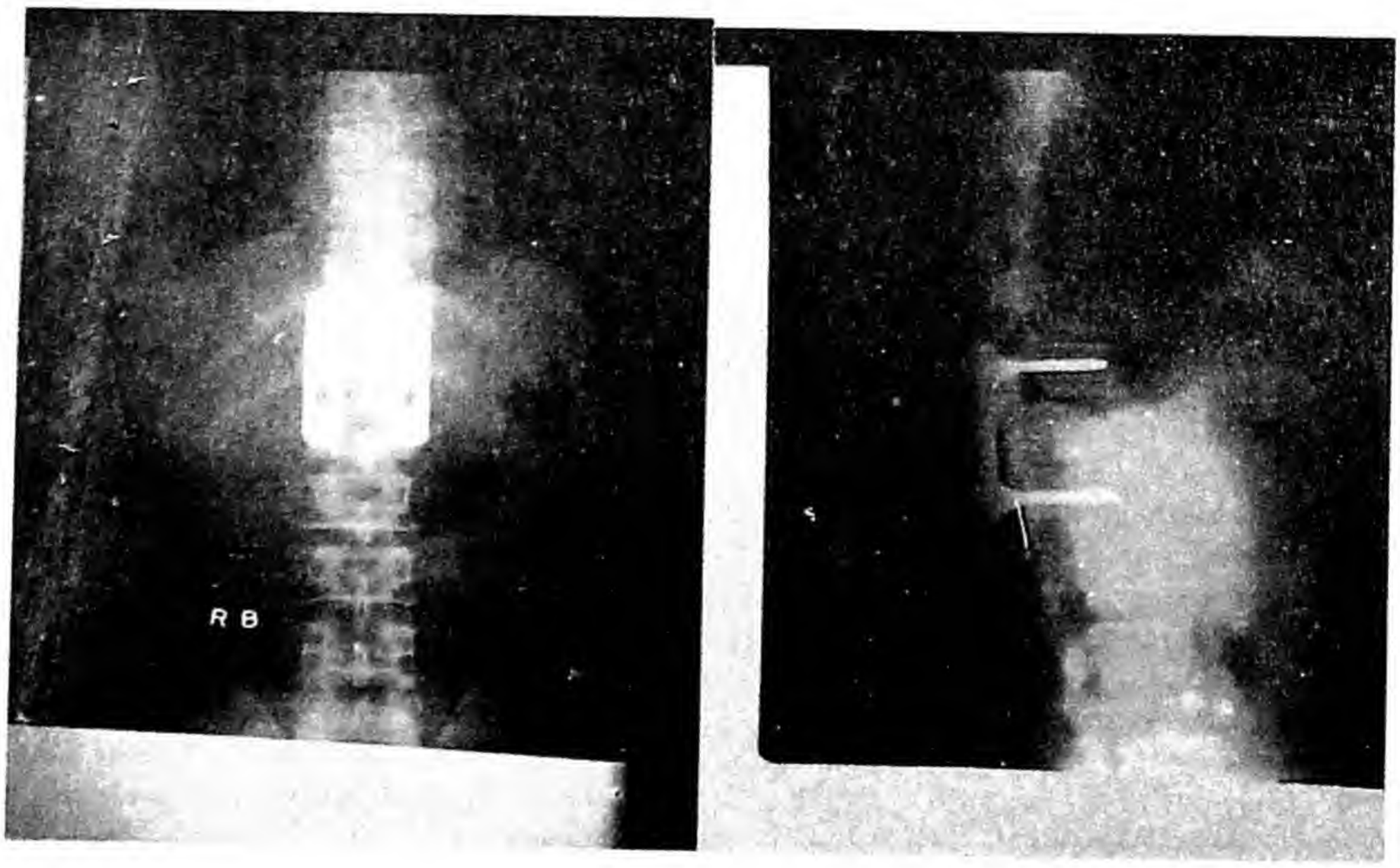


Figure2.Post-Op(ap/lat).Burst compression #D12.



was given.Patients with neurologic deficit were initially catheterized using foley's catheter.

A routine radiographic evaluation was done by AP &LAT. VIEWS.CT scan was done to know about any retropulsed fragments in the canal.Stability of the fractures was determined using the checklists suggested by WHITE AND PANJABI [3]. Fractures were classified on plain radiographs .The angle of kyphosis,the amount of translation were measured on plain radiographs and recorded for comparision postoperatively and at follow up.

The risks and benefits of the surgery were explained to each of our patients.Once the decision to operate was made,patients were taken to the operating room for the procedure.The patients were positioned in a prone position on soft blocks.A standard posterior midline approach to the spine was used to expose the spine one level above and one level below the site of injury after confirming the level of injury by c-arm.Once the osseous structures were adequately exposed,then the pedicles were prepared for pedicle screw placement using a stefffee awl.Pedicle entry points were identified using ROY-CAMILLLE [4] method of intersection.Smooth 'k'wires were inserted into the pedicles and verified by c-arm.Then the screws were driven in using a box spanner.We have used 4.5mm and 5.5mm steffee pedicle screws of 36mm and 38 mm lengths.Adequate length steffee plates were contoured and placed over the screws.A gentle and gradual distraction was performed using a mechanical distractor to correct the kyphosis and to achieve indirect reduction of any retropulsed fragment in the canal.The plates were locked over the screws using the tapered and the hexagonal locking nuts.A standard posterior iliac crest graft was taken and placed in the bed prepared for it.Wounds were closed over drains.Subcutaneous drain was used in the spinal wound.Patients were neurologically tested before leaving the operating room.Patients were kept flat for a period of 24 hours after the surgery.Patients were mobilized with ASH braces as early as possible.Patients were discharged from the hospital when they were safely ambulatory.Patients were advised to wear the ASH brace for a period of two months.Patients were followed up in the out patient department at 3weeks,3months,6months,1 year.

A comparative radiographic analysis was performed using pre-op,post-op and follow up x-rays.Sagittal translation and degree of kyphosis were measured and compared.The instrumentation was carefully analysed for any failure in the form of bent or broken screw.Also screws were looked for any backward migration.A comparative analysis of the FRANKEL [7] grades was done using the pre-op,post-opand follow-up neurologic status.

Table:1.

NO.OF PATIENTS: 20	
MEN:	16(80%)
WOMEN:	04(20%).

Table:2.

Age Group:	
Min.	18 years
Max.	46 years.
Avg:	32 years

Table:3.

Leel of Injury:	
thoracolumbar:	14(70%)
Lumbar:	06(30%)

L2---------3
L3---------2
L4---------1.

Table:4

Type of Injury:	
Brust #:	15(75%)
#-DISL:	05(25%)

Table:5

Kyphosis:	
Post-OP:	Av. 7.5 DEG
Followup:	Avg. 6.5 DEG

Table:6

Pre-OP:	Ag: 9.1 mm
Post-OP:	Avg. 2 mm

Table:7

NEUROLOGIC STATUS(FRANKELGRADE).

GRADE:	PRE-OP.	FOLLOW-UP.
A	3	1
B	-	2
C	3	-
D	4	1
E	10	16.

OBSERVATIONS AND RESULTS:

Twenty patients(16men-4 women) Table:[1] were analysed with average age of 32 years(18-46 years) Table:[2]. Our time to follow up averaged 7.5 months(3-12months).The cause of injury in all was fall from height.All fractures were between T11 &L5 Table:[3]. 70% were thoracolumbar injuries and 30% were lumbar injuries.75% were burst #'s and 25% were #-dislocations Table:[1].All patients had two motion segments(one above,one below)instrumented.The average blood loss was

600cc.The average operating time was 180 minutes.Average blood replacement was 1 unit.Average time from injury to surgery was 7 days.Patients were discharged from hospital on an average of 10 days(7-14days)

RADIOLOGICAL ASSESMENT:

We have computed the changes in kyphosis from pre-op to post-op values and from post-op to follow up values.We believe that initial correction and loss of correction at follow-up are the key values.Post-op kyphosis improved at an average of 7.5 degrees and at follow-up examination angle of kyphosis was at an average of 6.5 degrees.Thus 1 degree of correction was lost at follow-up Table:[5].The average translation was 9.1mm (5-18mm) initially and at follow-up it was 2mm(1-3mm) Table:6.There was no loss of translation from post-op values.

NEUROLOGIC INVOLVOMENT(FRANKEL GRADES):[7]

Ten of our patients had neurologic deficit of different frankel grades.Three patients had Grade-A.Two improved by one frankel grade to Grade-B,and one persisted with Grade-A.Three patients had Grade-C,Two improved to Grade-E and one to Grade-D.Four of our patients had grade-D intiallyand improved fully Table:[7].

COMPLICATIONS:

In one of our patients ,there was backward migration of one screw,because of smaller length of screw.We had missed the pedicle in two screws in which they were placed laterally.In our series till the last follow-up we had no implant failure.One patient had developed Grade-1 pressure sore which was treated with daily dressings and antibiotics and healed completely.

DISCUSSION:

Surgical stabilization of spinal injuries enables early mobilization,easy nursing care,and better rehabilitation of these patients of spinal injury.Pedicle screw fixation addresses segmental control of coronal,sagittal and axial alignment.Loss of intial correction after pedicle screw instrumentation is reported by many authors SASSO et al [9], and many others.Another pedicle related concern is screw placement,the most significant concern is "miss rate" reported anywhere from 10-28.8%.in our series it was 2.5%(2 screws out of 80 screws).Also we feel the method of ROY-CAMILLE [4] for pedicle entry is usefull in the lumbar spine as we found difficulty in locating pedicles in the thoracic spine by this method.One of the screws in a patient had backedout ,which we feel was because of inadequate length.We feel the screw if passed into the body upto the centre is adequate to increase the pull out strength of the screw.Till our last follow up we had no implant failure which has been reported commonly,we need to follow up these patients for more period of time regarding it.

In conclusion of this study which is no doubt a preliminary one, we feel STEFFEE [5] instrumentation is a favored system for stabilization of spinal fractures, as it provides a stable and rigid fixation, thus aligning the spine anatomically. Surgically it is less extensive construct that provides for immediate mobilization, reduces hospital stay, which is a very important factor in our setup and has a high patient satisfaction with a rapid return of best possible function..

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CLINICOPATHOLOGICAL STUDY OF PRIMARY SALIVARY-GLAND TUMORS IN KASHMIR

Shafkat Ahmad; Mohammad Lateef; Rouf Ahmad

ABSTRACT: *The study was undertaken for a period of two years from August 1998 to August 2000 with particular reference to age ,sex,site and histological types as per WHO classification.*

Out of 100 cases diagnosed on F.N.A.C. histopathological examination (HPE) was done only in 66 cases .Diagnosis correlated with FNAC diagnosis in 65 cases with an accuracy of 98.4%.Tumors were analysed according to the age, sex, site and histological type .Principal site was the parotid (70%).Pleomorphic adenoma(73%) formed the largest group of tumors in most sites. Benign tumors were common in 3rd & 4th decades while as malignant tumors were more common in 4th & 5th decades. Painless swelling was the commonest presentation and was present in 99% cases

KEY-WORDS: *Salivary glands, Major salivary glands, Minor salivary glands, Tumors.*

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INTRODUCTION:-

Salivary gland tumors comprise less than 3%of all tumors of head and neck.About 80% are located in the parotids,10% in the submandibular glands and the remainder being distributed between the sublingual and the countless minor salivary glalnds.[1-5] Benign tumors of the salivary glands occur in the age group of 30 – 70years. Malignant tumors are more frequent in women than men [6,7]. The peak incidence for malignant tumors is 6th and 7th decades.[8] Salivary gland tumors have a high incidence in the Eskimos and atomic bomb survivors of Japan[1,9].Several other predisposing factors have been postulated including race ,diet , occupation,E.B.virus etc.Present study was carried out to know the annual incidence and clinico-pathological profile of these tumors in this part of the country.

MATERIALS AND METHODS :

This study was carried out on patients attending ENT department of Govt. Medical college, Srinagar from August 1998 to August 2000.A detailed history including ,age, sex, residence, occupation and the clinical symptomatology was taken.FNAC was done in all patients suspected of having a salivary gland tumor in the cytology section of the Department of pathology of Govt. Medical College, Srinagar. In those patients who underwent any kind of surgery, routine investigations like haemogram, kidney function tests,X-ray chest and ECG was done. HPE was done only in 66 cases who underwent some kind of surgery.

OBSERVATIONS:

1. Tumors were observed in the age range of 46days to 80 years.Male to female ratio was1.17 : 1.0 .The highest incidence was in the 3rd to 4th decade in benign and 4th to 5th decade for malignant tumors (table- 1).
2. 99% patients presented with a swelling or palpable mass pain was present in 15 cases (15%) out of which 10 were malignant and 5 benign.
3. The benign tumors constituted 86% and malignant tumors 14% of primary salivary glands tumors.Parotid gland was involved in 70% of cases followed by submandibular gland (18%) and minor slivary glands (in 12% cases). Palate was the commonest minor salivary gland tumor site (7% total).
4. Pleomorphic adenoma was the commonest tumor (73%) of all primary salivary gland tumors and parotid was the commonest site (57%) table-2.
5. Malignant tumors were also common in parotid glands constituting 50% of all malignant salivary gland tumors (28.5%). Adenoidcystic carcinoma was the most common malignant primary salivary gland tumor (35.7%) Table-2.
6. There were total five recurrent salivary gland tumors. Four cases in parotid and one case in parapharyngeal space. All these cases had undergone excision enucleation for pleomorphic adenoma in the past (1-4 year duration). Out of these four excision enucleation were done by general surgeons. Thus excision enucleation (partial superficial parotidectomy) in general and especially by general surgeons seems to be associated with higher recurrence because of inadequate and inaccurate excision enucleation of the tumor

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Table No.2: Site distribution of salivary gland tumors (FNAC).

Tumor	Parotid	Subman-dibullar	Palate	Lip	Cheek	Nasal cavity	Paraph-a-ryngeal Space.
BENIGN TUMOR							
Pleomorphic Adenoma	57	9	4	1	1	-	1
Myoepithel-ioma	-	-	1	-	-	-	-
Haemangio-ma	2	-	-	-	-	-	-
Lymphangi-oma (Fig 3)	1	1	-	-	-	-	-
Lipoma	2	3	-	-	-	-	-
Cystadenoma	1	-	-	-	-	-	-
Neurofibro-ma	-	1	-	-	-	-	-
MALIGANT TUMORS							
Mucoepiderm-oid carcinoma	3	-	-	-	-	-	-
Adenoid cystic Carcinoma	1 (Fig-4)	1	1	-	-	2	-
Acinic cell Tumor	-	1	-	-	-	-	-
Ex-pleomorphic Adenoma	1	1	-	-	-	-	-
Adenocarc-inoma	2	-	1	-	-	-	-
Total	70	18	7	1	1	2	1

7. Out of 100 patients, 64 underwent surgery, 1 case of adenoid cystic carcinoma of nasal cavity received radiotherapy and one case of haemangioma local steroids. Rest of the patients did not report for surgery.

Table No. 1: Age and sex distribution of benign and malignant salivary gland tumors.

Age (years)	Malignant	Male	Female	Benign	Male	Female
0-10	1	-	1	4	4	-
11-20	1	-	1	11	3	8
21-30	1	1	-	21	8	13
31-40	3	1	2	23	16	7
41-50	2	2	-	16	9	7
51-60	4	4	-	8	5	3
61-70	1	-	1	3	1	2
71-80	1	-	1	-	-	-
Total	14	8	6	86	46	40

DISCUSSION:

Only a few recorded analysis of salivary gland tumors based on significantly large number of cases are published from India and in particular Kashmir. The present study involves all cases of primary salivary gland tumors which reported in the Department of ENT, Govt. Medical College,Srinagar during August 1998 to August 200

Neoplasms of salivary glands are uncommon [6,7,10], the annual incidence appears to be higher in western publications which may be due to the fact that these were based on the centralized treatment centres. In our study the incidence is close to western data because data is from a centralized treatment centre.

Salivary gland tumors were observed in all ages but the highest incidence was in 3rd and 4th decade for benign tumors and 4th and 5th decades for malignant tumors.The average age for benign tumors was 35.7years and 42.4 years for malignant tumors, which is close to 32.7 years for benign 42.4 years for malignant tumors as reported by Narinder Singh et. Al.[3].Male to female ratio was 1.17 : 1.0 in comparison to the most studies where females out-numbered males.[1,2,3] This is because mostly females being confined to their homes don't come for treatment. The incidence for benign salivary gland tumors (86%) is higher than the malignant tumors(14%). The duration of symptoms ranged from 45 days to 25 years . The age range reported by Chan et.al[11] (1992) is 25 years to 83 years. The commonest symptom was a painless swelling which was present in 99% cases. Similar observations were made by Loke.[5] Wallace et.al.[1] reported the range of tumor size in his series to be 1.8-4cm whereas Sharkey[8] reported a mean size ranging from 0.5 – 7cm. In the present series, mean tumor size ranged from0.5cm- 25.5cm.

All the100 cases in our study were subjected to FNAC, as it is a quick, simple, rapid, inexpensive and a harmless procedure.

HPE was done in 66 cases out of 100 cases . HPE diagnosis correlated with FNAC in 65 cases with a diagnostic accuracy of 98.4%. thus FNAC is recognized as a practical, simple and a useful technique for the diagnosis of the salivary gland tumors.[10] There were total 5 recurrent

salivary gland tumors.4 cases were in the parotid glands and one in the parapharyngeal space. All these cases had undergone excision- enucleation for pleomorphic adenoma in the past(1-4 years duration). Out of these 4 excision – enucleations were done by general surgeons.Thus recurrence was associated with excision – enucleation in general and especially by general surgeons as compared to other radical procedures because of inaccurate excision of tumor. Narinder singh[3] reported recurrence in 10 cases in benign tumors and 8 malignant tumors .No reccurene was seen in benign tumors of the submandibular gland as the as the complete excision was done .Our observations are not consistent with most authors because of short follow up period.

Patients are followed at 6 monthly intervals . one patient in our study died after 2 years follow up.

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SONOGRAPHIC APPEARANCE IN INTESTINAL ASCARIASIS

Ishtyak Ahmed Mir; Nazir Ahmed Wani; A..G. Ahangar; Patnaik Rekha; Khalida Saleem

ABSTRACT: Sonographic examination of the abdomen was performed in 100 patients admitted with features of acute intestinal obstruction caused by ascariasis. In 72 patients sonography of the abdomen was of no help. In 28 patients ascaris lumbricoides were seen in the gut. The sonographic appearance of worms was noted as coiled up masses of worms which were hyperechoic and with out acoustic shadowing and linear hyperechoic shadows of worms in fluid filled bowel. 92 patients were managed conservatively and 8 patients underwent surgery.

Key Words: *Ascariasis, Sonography.*

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INTRODUCTION

Intestinal ascariasis is a frequent cause of paediatric intestinal disease in Kashmir valley, India[1,2]. The principal surgical complications are caused by obstruction and perforation of intestinal wall by adult ascaris[3]. Majority of these patient with bolus obstruction of the gut can be managed conservatively provided the cause of obstruction is ascariasis[4-7]. Since there is no specific method for diagnosis of surgical ascariasis, controversy still exists regarding conservative and surgical management moreso about when the conservative treatment should be abandoned and the patient subjected to surgery. In the present study, we prospectively evaluated the role of sonography in the diagnosis of intestinal ascariasis and its utility in monitoring the disintegration of worm masses in intestines. Serial abdominal scans help to pick up surgical complications well in time and also to decide about conservative and surgical treatment. Majority of these patients have bolus obstruction in terminal ileum near ileocaecal valve. It is presumed that leaving aside the closed loop obstruction caused by ascariasis., fluid filled segments of bowel can also be seen in bolus obstruction in few patients. The diagnosis of small bowel obstruction by Scheible W et al (1979)[8], and sonographic patterns of distended fluid filled bowel by Fleischer AC et al (1979) [9] help in demonstrating fluid filled bowel. It is in these fluid filled segments of bowel that coiled up worm masses, disintegration of worms during conservative treatment, and single worms can be demonstrated.

MATERIAL AND METHODS

The study was conducted on 100 patients admitted with acute intestinal obstruction due to intestinal ascariasis. Pain abdomen, vomiting and constipation were the common triad of symptoms. Clinical findings of significance included distension abdomen and palpable worm masses which disappeared during conservative treatment. Baseline investigations and x-ray abdomen standing and lying down were contemplated in all. Patients with gasless abdomen on x-ray but with clinical features of intestinal obstruction were considered ideal for abdominal scans. The sonographic examination of the abdomen was performed using a B mode realtime ultrasound scanner (ALOKA SSD 280) with 3.5MHZ convex linear and 5MHZ sector transducers. The transducer was placed longitudinally and transversally on the anterior abdominal wall with the patient lying supine. Patients were also scanned in semi-upright position. Ileum (which is identified by smooth featureless walls) was fluid filled in 20 patients, followed by closed loop obstruction (confirmed at laparatomy) of jejunum in 3 patients distended loops in semiupright position 5 patients.

Sonographic evidence of atonic, fluid filled bowel with coiled up masses of worms and linear hyperechoic shadows of ascaris in distended fluid filled loops were considered absolute indications for surgery. In patients with out sonographic evidence of ileus, but fluid filled bowel with ascaris worms conservative treatment was given with more conviction. Sonographic appearance of bolus of worms in distended fluid filled bowel was, coiled up masses of worms which were hyperechoic and without acoustic shadowing.

The disintegration of these masses was noticed during conservative treatment by serial abdominal scans. All these patients received intravenous fluids, antispasmodics and anti-helminthic therapy. In addition, antibiotics and enemata were used in selected group of patients only. Ascariasis as the cause of obstruction in all the 100 patients was

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confirmed by the patients response to conservative treatment. Disappearance of worm masses, relief in pain, vomiting and constipation. Passage of worms per rectum of varying size and at laparatomy.

RESULTS

Sonographic appearance in patients with intestinal ascariasis were as follows*: (a) distended fluid filled bowel segments in (16 patients); (b) atonic fluid filled bowel (3 patients); (c) coiled up masses of worms which were hyperechoic and without acoustic shadowing (9 patients); (d) linear hyperechoic shadows of ascaris in cross section (12 patients); (e) characteristic movements exhibited by these echogenic structures in fluid filled bowel (8 patients); (f) closed loop obstruction with coiled up masses and linear hyperechoic shadow in (3 patients). *More than one finding was present in a patient.

Surgical finding were bolus obstruction (6 patients) all in terminal ileum, volvulus with gangrene of jejunum (2 patients) volvulus without gangrene (2 patients). Enterotomy was done in two and milking of worms from ileum to caecum in 4 patients. Resection with end to end anastomosis was done in 2 patients.

DISCUSSION

Plain x-ray abdomen and contrast studies of gut are good tools to demonstrate worms in gut and their complications [10-13]. However, these investigations have their own limitations, as plain x-ray may help visualize worm masses, air fluid level, but is of no use in cases of gasless abdomen. Contrast studies cannot be performed unless one is sure there is no visceral perforation and closed loop obstruction, moreover can not be done in patients not responding to conservative treatment. The hallmark of intestinal obstruction is the intraluminal accumulation of fluid (Scheible W et al 1979)[8]. The presence of air makes it easier to visualize dilated fluid-filled loops on plain radiographs,[13] but when gas is absent the fluid filled loops may be difficult to identify. In these situations sonography is the investigation of choice. In Kashmir India where ascaris lumbricoides is the commonest cause of intestinal obstruction in paediatric age group, it is very important to know that ascaris lumbricoides is really the cause of ailment. If the cause of obstruction is ascariasis without sonographic evidence of atonic, closed loop obstruction, a trial of conservative treatment can be given. The fact is that ascaris lumbricoides can cause features of acute intestinal obstruction usually by a bolus of worms in ileocaecal region. Majority of these patients can be managed conservatively because the worm masses disintegrate and patient can get relief from symptoms. However, if the cause of intestinal obstruction is not ascarideal and the sonographic evidence is of atonic, fluid filled loops immediate surgery is needed.

Peck R.J (1990)[14] gave the ultrasonographic diagnosis of intestinal ascariasis. Their patient had fluid filled loops of bowel and within one loop ascaris lumbricoides was present. The patient was operated even through he had only one worm at sonographic exam and laparatomy.

CONCLUSION

We hereby conclude that ultrasonography helped in establishing ascariasis as the definite evidence of ailment in 28 patients. Sonographic criteria for surgical exploration was made in 8 patients though in three patients surgery could have been avoided by prolonging the period of conservative treatment. We emphasize on sonographic examination of abdomen in all patients where ascariasis is very predominant especially in paediatric age group.

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POSTEROLATERAL THORACOTOMY COMPLICATING PARAPLEGIA

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Abstract; *Paraplegia complicating thoracotomy has been reported in literature in mid forties. However in sufficient data are available about the incidence of such a catastrophic complication. In the present study five cases of paraplegia following thoracotomy are presented. Pneumonectomy, lobectomy for bronchogenic carcinoma. decortication for tubercular empyemas and thoracotomy for ductus ligation constituted one, one, two and one patient respectively. Two patients died in post operative period, two died in follow up and one patient is still on follow for the last twelve years.*

Key words: *Posterolateral thoracotomy, Paraplegia*

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INTRODUCTION

Paraplegia complicating thoracotomy for aortic operations is a well recognised catastrophic event. Less well recognised is the incidence of paraplegia after thoracotomy for pleural or pulmonary disease and in surgical procedures for malignant hypertension.

Injury to the spinal cord with resultant paraplegia usually results from attempts to control persistent bleeding at the posterior angle of intercostal incision or at the site of removal of a portion of vertebrae.

MATERIALS AND METHODS

The study was conducted in the department of cardiovascular and thoracic surgery SKIMS Soura Kashmir, India. All the patients were recorded with regard to type of disease, operations performed age and sex and the complication of paraplegia. Every attempt was made to find out the most probable cause with regard to extensive dissection in posterior angle of incision, use of electrocautery and oxidised cellulose. CT scan combined with myelo CT was the investigation of choice. Decompression for fractured vertebrae, extradural hematoma and removal of oxidised cellulose was the surgical modality. Some ways and means were devised to prevent the catastrophic complication.

OBSERVATION

The present study has shown that thoracotomy for seemingly innocuous conditions such as paraplegia following surgery for tubercular empyema, and ductus arteriosus and other lung and pleural disease is not only unusual but also unacceptable. The paraplegia recorded in present series is given in table I. The neurologic deficit was detected with in 1 to 72 hours after surgery. All these patients had extensive dissection in posterior angle of incision, all the measures were used to stop bleeding from

Table 1. Thoracotomy complicating paraplegia in present series

Age (yrs)	Sex	Diagnosis	Operation performed	Neurologic loss	Level	Outcome	Comment
57	M	Tubercular empyema	Decortication	Paraplegia	T6-T7	Not improved	Died of septicaemia
65	M	Bronchogenic carcinoma	Left lower lobectomy	Paraplegia	T6-T7	Not improved	Died two year later of metastasis
12	F	PDA	Ligation	Paraplegia	T6-T7	Not improved	Still on followup
59	M	Bronchogenic carcinoma	Left pneumonectomy	Paraplegia	T6-T7	Not improved	Died 4½ year later in a RTA
47	F	Tubercular empyema	Decortication	Paraplegia	T5	Not improved	Died of bleeding diathesis

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the posterior angle of posterolateral thoracotomy, also in all these five patients there were fractures of adjacent ribs at posterior angle to get wide exposure for exposure of bleeders and or for dissection of the underlying pathology. CT myelogram was done in all the patients. Fracture of vertebrae T8-T9 was observed in one patient, complete block at T8-T9 was documented in two patients. In one there was complete transection of cord and in one no significant hematoma or block was noticed. Surgical decompensation attempted in three was of no help.

REVIEW OF LITERATURE

Paraplegia complicating posterior thoracotomy is rare but catastrophic. The study comprises 45 cases, 5 of our study and forty reported cases (Table 2). Paraplegia complicating thoracotomy for aortic operations is a well recognized catastrophic event. Its incidence is well-documented in surgery of atherosclerotic and dissecting thoracic aortic aneurysms, thoraco-abdominal aortic aneurysms, abdominal aneurysms, and coarctation of the aorta.

Paraplegia is one of the most dreaded complications of aortic operations. The more posterior the incision was toward the vertebrae, the greater the chance was for injury to the spinal cord. Bleeding at the costovertebral angle. Attempts at controlling the bleeding by electroacutery or by packing the wound with oxidized cellulose have been implicated in the causation of this complication. Other factors implicated in the causation of paraplegia include intraoperative blood loss, hypotension, ligation of intercostal vessels that might be supplying the arteria magna of Adamkiewicz, thrombosis of anterior spinal artery, epidural anesthesia, and epidural hematoma.

DISCUSSION

The incidence of paraplegia after thoracotomy is not well known. Our observations are at variance with with other reported series[1,2] because in our experience of 33

Table II: Thoracotomy complicating paraplegia - reported cases from review of literature

Author	year	Diagnosis	Operton	Nerologic Level Loss (paraplegia)	Out come
Mosberg et al	1944	Malignant Hypertension	Bilateral supradiaphragmatic and Lower dorsal sympathectomy	T-12	Improved
Mosberg et al	1944	Malignant Hypertension	Bilateral supradiaphragmatic and lower dorsl sympathectomy	T-12	No imporvement
Mosberg et al	1946	Malignant Hypertension	Left thoracolumber sympathectomy; right thoracolumber sympathectomy	T-12	Died
*Bassett (2 cases)	1948	Malignant Hypertension	Sympathectomy	T8-T10	No improvement
*Mosberg et al (3 cases)	1954	Malignant Hypertension	Sympathectomy	T8-T10	No improvement
Billing and Robertson	1955	Tuberculous empyema	Drainage of tuberculosis cavity-left chest	T10	Died 2 months later
Nathan	1956	Malignant Hypertension	Thoracolumber sympathectomy	T-12	No improvement
Rouques and Passelecq	1957	Pulmonary tuberculosis	Thoracoplasty right	T-6	Improved
Binet	1961	Tuberculous pyothorax	Pleuropneumonectomy	T-6/T-7	No improvement
Corbin	1961	Pulmonary T8	Thoracoplasty	Paraplegia	Not known
Hughes & MacIntyre	1963	Malignant Hypertension	Thoracolumber sympathectomy	T-9	Improvement
Thomeret	1965	Pulmonary tuberculosis	Thoracoplasty after pneumonectomy	T-5-T-6	Improvement
Henson & Parsons	1967	Trauma	Left Lower lobectomy	T-6	No improvement
Mathew & John	1970	Bronchiectasis	Left pneumonectomy	T-4	Improved
Bennett	1975	Benign lung lesion	Left upper lobectomy;	T-6-T-7	Unknown
*Merlier & Thevenet (7 cases)	1980	Pulmonary tuberculosis	Thoracoplasty		
		Pancost tumor	Right upper lobectomy		
		Traumatic pyothorax	Thoracoplasty		
		Pulmonary tuberculosis	Left pleuropeumonectomy	T-4-T-5	No improvement
		Peptic esophagitis	Left thoracotomy Nissen operation		
		Neuroma 4th intercostal space	Excision of neuroma		
		Ganglioneuroma 8th intercostal space	Excision of ganglioneuroma		
Nancekivell	1985	Bronchogenic Ca	Right pneumonectomy	T-5	No improvement
Tashiro et al	1987	Bronchogenic Ca	Right upper lobectomy;	T-5	Brown-Sequard syndrome (improvement)
Perez-Guerra & Holland	1988	Bronchogenic Ca	Left pneumonectomy;	T-5	No improvement
Johr & Salathe	1988	BronchogenicCa	Left pneumonectomy	T-5/T-6	Died
Batellier et al	1989	Bronchogenic Ca	Right upper lobectomy;	T-5	No improvement; died
*Short (2 cases)	1990	Bronchogenic Ca/	Right upper and middle lobectomy	T-5/T-6	No improvement
		Bronchogenic Ca	Right lower lobectomy		
Short	1990	Bronchogenic Ca	Right upper lobectomy right spastic monoplegia	T-5/T-6	Left leg improved;
*Wada et al (2 cases)	1993	Bronchogenic Ca	Right upper lobectomy;	T-5	Improved
Attar et al	1995	Bronchogenic Ca	LU lobectomy	T-6-T-7	Not improved Died
Attar et al	1995	Bronchogenic Ca	LL lobectomy	T-6-T-7	improved
*Attar et al (3 cases)	1995	Pulmonary tuberculosis	LU lobectomy	T-6-T-7	Not improved
		Tuberculous empyema	Decortication	T-6-T-7	Not improved
		Stab wound	Control of bleeding	T-6-T-7	Not improved

* Multiple patients reported by same authors had different or same changes but underwent different or same surgical procedures but had same level and similar outcome

patients having dorsal or lumber sympathectomy none developed paraglegia. Our observations are in consistence with many authors[3-5]. All of them have reported paraplegia after pneumonectomy radical pulmonary section and post pneumonatomy epidural hematoma. The use of oxidised cellulose in all cases of present study has also been reported[6]. Based on our experience of about 3943 thoracotomies it is believed to be around 0.11 percent which is quiet high and unacceptable, but could be because of two reasons, firstly Attar et. al 1995[7] had not included any of PDA patient in their study which is a part of aortic surgery, and secondly none of their patients had massive, bleeding, hypotension and they had not used oxidised cellulose in any of their patient. In fact the PDA patient included in the study is because she developed this complication as a consequence of posterolateral thoracotomy and not due to surgery on ductus. As is evident from table II dorsolumbar sympathectomy for malignant hypertension was the commonest reported cause of paraplegia in 1940's. But in fifties and sixties, surgery for pulmonary tuberculosis was the commonest cause. Myelo CT as the investigation of choice and emergency decompression is the accepted mode of management[4,6-9]. Hospital mortality of two patients was because of re-exploration septicaemia and bleeding diathesis.

The greater chance of injury to spinal cord are - more posterior the incision towards the vertebrae, bleeding at the costovertebral angle, haphazard attempts at controlling the bleeding by electrocautery, packing the wound with oxidised cellulose, intraoperative blood loss, hypotension, ligation of intercostal vessels, thrombosis of anterior spinal artery, epidural anaesthesia and epidural hematoma. In the present study it can be said with certainty that the complication occurred because of extensive dissection in and around vertebral region, maximum use of cautery and oxidised cellulose, adjacent rib fractures at posterior angle while acting adequate exposure and ligation of intercostal vessels.

Of great concern is the paraplegic female who has been attending our OPD from last 14 years but we don't have a solution for her. It is emphasized that all the preventive measures can be taken/adopted and that should not limit the field of surgery in modern time and prevent this catastrophic complication.

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ULTRASONOGRAPHY IN DIAGNOSTIC EVALUATION OF GYNAECOLOGIC PELVIC MASS

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Abstract: *Ultrasound is used to delineate the size, consistency and structure of origin of pelvic mass. The diagnosis of pelvic mass can be inferred in light of appropriate history and confirmatory sonographic findings. Ultrasound gives information about function and morphology of abnormal organ when pelvic examination is un-remarkable and difficult.*

The aim of the study was to evaluate the diagnostic reliability of ultrasonography in various gynaecologic pelvic masses. 55 patients with a variety of gynaecologic pelvic masses were evaluated. In 33 patients (60%) the Sonographic diagnosis was thaught to be confirmatory of clinical disease and in seventeen patients (30.9%) it revealed the actual status of patients. In 5 patients (9.1%) the diagnosis was characterized as misleading.

Key words: *Pelvic mass, Sonography.*

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INTRODUCTION

Over the past decade advances in Radiological Technology with subsequent introduction of imaging modalities changed the gynaecologic evaluation of female pelvis. Gynaecologic ultrasound was first used by Donald Etal in 1958 in diagnosis of abdominal masses and increased experience resulted in wide spread use of this technique as a diagnostic and surgical tool in gynaecologic practice.

The evolution of ultrasound through A-scanning, bitable scanning and static B scanning limited the use of gynaecologic ultrasound and it is with the advent of real time mechanical sector ultrasound that gynaecologic ultrasound and ovarian scanning have become widely used in day to day practice.

The current methods of pelvic sonography in use are transabdominal real time scanning and transvaginal real time scanning. In transabdominal scanning most often uterus and ovaries are visualized by using 3 MH transducer at a depth 10-15 cm through urinary bladder whereas with transvaginal sonography the same structures are visualized at depth 1-8 cm and 5-7 MH transducers are used. Transvaginal sonography unquestionably provides excellent depiction of pelvic organs[1-6]. A major disadvantage of transvaginal ultrasonography is that effective focal zone of transducer is shot, masses that are beyond the range of probe will not be clearly defined or will be missed completely.

At present the role of ultrasound for detection and evaluation of pelvic mass is well established. Ultrasonography has become an accepted part of modern gynaecological practice. Ultrasonographic evaluation is an important adjuvant to clinical evaluation of gynaecologic pelvic masses. There is no question of its value of detecting and localizing number, structure of origin and position of pelvic masses .In some instances the type of tumor can be detected. Ultrasound is used in distinguishing the origin and position of pelvic masses. In some instances the type of tumor can be detected. Ultrasound is used in distinguishing the origin of pelvic masses whether uterine or adnexal and whether pelvic mass is cystic, solid or mixed[7-8].

Pelvic masses that are overlooked on physical examination will be identified by ultrasonographic examination. Conversely the identification of small myomas, ovarian enlargement and physiological cysts may lead to increased patient concern and even operations that might be unnecessary. However the drawbacks of sonography include technicai limitation caused by patient habitues, operator dependence and techniques inability to provide specific characterization.

MATERIAL AND METHOD

A study of 55 patients with a variety of gynaecologic pelvic masses was made during January 1994 - January 1995 in Abu-Arish General Hospital. The detailed clinical history was taken and general and local pelvic examination was performed for all patients with various palpable pelvic masses on bimanual pelvic examination. Pelvic ultrasonography was performed for all patients by real time equipment with 3.5 MHz transducer using transabdominal route as under. In order to have full bladder patient was asked to drink 2 liters of water one hour before examination

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and was advised not to empty her bladder until after scan was complete.

The patient was asked to lie on examination table in supine position leaving lower abdomen and supra pubic area uncovered just sufficient to allow the examination to be performed. Acoustic gel was applied to patient's lower abdomen. The transducer was placed in midline above bladder at pubic area. The size, location of uterus, cervix, vagina and ovaries were determined and relation of pelvic masses to these structures noted. The nature of pelvic mass whether cystic or solid complex was assessed. The bladder contour and any fluid in pouch of Douglas noted. Scans were obtained at 1 or 2 cm interval in transverse and saggital planes. Final diagnosis was confirmed from operative findings.

Table I: - Clinical distribution of pelvic mass

Clinical diagnosis	No. of patient
Leiomyoma	17
Haematometra	03
Hydatidiform mole	04
Uterine malignancy	01
Adnexal cyst	19
Tubal ectopic pregnancy	06
Pelvic inflammatory disease	04
Polly-cyst ovarian disease	01
Total	**55**

The diagnosis established by sonographic evaluation was considered to be confirmatory, if clinical diagnosis was reaffirmed. If actual status of patient was established by sonography the interpretation was deemed to be diagnostic. If sonographic interpretation did not reveal the actual status of patient the diagnosis was classified as misleading.

Table II: - Clinical distribution of pelvic mass

Diagnosis	Confirmatory	Diagnostic	Misleading	Total
Leiomyoma	12	04	01	17
Haematometra	*03*	*0*	*0*	*03*
Hydatidifen mole	03	01	0	04
Uterine Malignancy	01	0	0	01
Adnexal cyst	10	08	01	19
Tubal ectopic pregnancy	02	03	01	06
Inflammatory disease	02	0	02	04
Polly cystic ovaries disease	0	01	0	01
Total	33	17	05	55

Table III: - Distribution of cases with misleading Ultrasound diagnosis

Ultrasound diagnosis	Final diagnosis	No. of patients
Leiomyoma	Adenomyosis	01
Adnexal cyst	pelvic adhesions	01
Tubal pregnancy	Ruptured corpus lutem cyst	01
Pelvic inflammatory disease	Ectopic pregnancy (less than 5 weeks)	01
Adnexal cyst	Tubal ectopic pregnancy (old)	01

RESULTS:

The clinical diagnosis of various pelvic masses is shown in Table I. The characterization of sonographic diagnosis is shown in Table II, from which it is evident that in thirty three patients (60.0%) the sonographic diagnosis was thought to be confirmatory of clinical disease and in seventeen patients (30.9%) sonography revealed the actual status of patients (9.1%). Sonographic did not reveal the actual status of patient and were characterized as misleading. Misleading sonographic diagnosis are shown in table III.

DISCUSSION:

In the present study an attempt was made to evaluate the diagnostic accuracy of sonography in various gynaecologic pelvic masses. From the above results it is clear that correct diagnosis was established in 50 patients (90.9%) and misleading in 05 patients (9.1%). Which is lower than Voss Etal[9] who reported predictive value of ultrasound diagnosis of specific disorder as 97%, whereas predictive value of sonographic examination that showed no apparent abnormality as 40% only.

Ronald Etal [10] confirmed the clinical diagnosis by ultrasound in 36.8% and sonography established the diagnosis in 59% of cases. Thus reporting correct sonographic establishment of diagnosis by ultrasound is 56% in staging the tumors of cervix uterus[11-12]. Some authors found pelvic sonography and clinical examination to be equal in accuracy for determination of size, position of pelvic mass and superior in prediction of solid or cystic nature of such masses.

After reviewing 300 cases of gynaecologic ultrasound diagnosis Queenan Etal (1975) found 74% to be confirmatory of referral diagnosis, 21% were thought to be diagnostic and 5% were classified misleading. When the pregnancy test is negative the differential diagnosis of gynaecologic pelvic mass in young female is leimomyoma, ovarian cyst and endometriosis. In cases with positive pregnancy test or available BHCG result will rule out pregnancy complications like ectopic pregnancy.

Myomas may be demonstrated by distortion of bladder or uterine contour. Clustered bright echoes will suggest calcification and produce distal acoustic shadowing. It is difficult to distinguish myoma by ultrasound from sarcoma or other uterine neoplasm. Obstructed drainage leading to Haematometra is seen on ultrasound as a centrally cystic, round, moderately enlarged uterus. Charles Etal[13] reported that sonographically enlarged uterine cavity in postmenopausal women (upper limit of antero posterior diameter 3cm and length 8cm) is indicator of malignancy.

They added that pelvic sonography is not screening test for uterine malignancy. The reported findings in postmenopausal uterus indicating malignancy are fluid filled obstructed uterus[14-15], the enlarged uterine cavity[16], the enlarged uterus and lobular uterus with mixed echo pattern.

The increased use of sonography in diagnostic evaluation of pelvic mass allows earlier diagnosis and better characterization of adnexal neoplasm. The experienced ultrasonographer can determine position, size and gross morphology of adnexal masses in almost every instance it is more difficult to determine exact tumor type.

Single or multiple clear cysts in only slightly enlarged ovary are probably physiologic. Large unilocular ones may be cyst adenomas.

Multiloculated cystadenoma, benign teratoma, endometriosis and corpora lutea usually have characteristic appearances. It is possible to suspect malignancy on the basis of ultrasonic image but a definite diagnosis can not be always made. Benacerref Etal[17] reported a 73% positive predictive value for excluding adnexal masses and 91% negative predictive value for excluding malignancy. Benign tumors usually have sharp well-defined margins and are more likely to be anechoic. Indistinct border and the presence of solid echoes pattern suggest malignancy and as echogenicity increases so does the possibility of malignancy although ascites is usually present when a malignant tumor involves peritoneum. There may be only a minimal amount of cul-de-sac fluid or none at all. Para-ovarian, broad ligament cysts have very thin compressive walls and are never surrounded by ovarian tissue. Since solid tumors are more likely to be malignant then simple cysts, the findings of a solid ovary greater than 5 cm in diameter should prompt an abdominal survey for signs of malignancy. Solid tumors include Brenner tumor, Granulosa cell tumor, theca cell tumor and fibromas.

Mixed solid and cystic ovarian masses on sonography makes it more likely to be malignant, especially if it is associated with ascites. One of common ovarian tumor with mixed component is germ cell derivative, dermoid cyst, which contains bone, teeth, hair and sebaceous material.

In hydatidiform mole ultrasound has classical snow storm appearance on B mode scanning. On real time the small vesicles and areas of haemorrhage are obvious with advent of real time sonography particularly with sector scanning, it become apparent that direct visualization of tubal pregnancy gestation sac outside the uterine cavity or rarely a definite extrauterine fetus could be visualized. According to Kimz etal[18] the criteria for ectopic pregnancy include absence of intrauterine sac with serum BHCG of more than 1000 mg/l and an adnexal mass and fluid in abdomen.

According to Anthey and Hadlock[19] sonography of female pelvis should not be expected to provide histologic diagnosis. However it is stressed to improve the clinical diagnostic skill and learn to use ultrasonography as a secondary rather than primary diagnostic tool. Thus ultrasound is useful in defining symptomatic or palpable pelvis mass as described above.

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ORIGINAL ARTICLE

JK-PRACTITIONER

EASY COST EFFECTIVE FIRST LINE TREATMENT FOR INFERTILITY

Abida Ahmad, MD;

Abstract: *The study was carried out on 88 patients of infertility irrespective of duration, type or cause. The patients were seen in the OPD of Obstetrics Hospital at Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar (SKIMS). A detailed history was taken and routine examination was done. All expensive and invasive investigations were deferred and patients were put on 5mg of folic acid and 100mg of Vitamin B_6 daily. It was found that 62 patients (70.45%) conceived within 4 months of treatment. Conception rate was more in primary infertility cases (76.39%), than in Secondary infertility cases (43.75%). Likewise conception rate was more in younger age group with marital life of 2-3 years.*

Key Words: *Infertility, Primary infertility, Secondary infertility, Folic acid, Vitamin B_6*

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Inability of a couple to conceive after one year of unprotected coitus with adequate coital frequency is labelled as infertility. It is a common cause for consultation with both the general practitioner and specialist affecting one in six couples. 80-90% of fertile couples will achieve a pregnancy within one year of trying and 95% within 2 years. Aetiology is usually multifactorial and varies with the duration of infertility. Aetiology at an early stage includes unexplained infertility (30%) (really delayed normal fertility); male factors (25%) (single most common defined cause); ovulatory failure (20%); tubal damage (15%) and endometriosis (5%).

Childlessness can be tragic to the married couple and most of the times a cause for marital discord. Hormonal medications and surgical interventions used for treatment of infertile women are very expensive. Drugs which are cheap, easily available, with no side effects and help the infertile women should be welcomed and tried as first line treatment for infertility.

In the present study we have tried to see the effectiveness of Pyridoxine (VitaminB_6) and folic acid in treating infertility.

Exact mechanism of action remains unknown and the probable mode of action of vitamin B_6 is that it acts as a cofactor in number of enzymatic steps of tryptophan metabolism.[1] Being vital for protein synthesis pyridoxine (vitamin B_6) in the form of pyridoxal phosphate has been postulated to increase the conservation of intraneural dopa to dopamine by acting as a coenzyme of dopa-decarboxylase. Consequently the vitamin increases the dopamine content in hypothalamus,[2] and thus helps in correction of hyperprolactenemia, which is a known factor for infertility. Folic acid helps in DNA synthesis during cell replication.[3] DNA synthesis in endometrial stromal cells is required for implantation[4] and deficiency of folic acid may lead to subclinical abortion before a pregnancy is diagnosed.

Material and Method

The present study was conducted on 88 infertile patients irrespective of type, duration and cause of infertility. Detailed history was obtained from the patient in OPD including age at the time of marriage, duration of marriage, past history of illness, general health, age at puberty, diet habits, drugs, any operations undergone, occupation, sexual life and menstrual irregularity. Routine physical examination and pervaginal examination was done. Routine investigations including husbands semen examination and USG pelvic organs was done. Simultaneously the patient was put on one Tab. of Fol-5 (folic acid 5mg) and one Tab. of B long (Vitamin B_6 100mg) continuously.

Observations and Discussion

Out of total 88 patients 72 patients had primary infertility and 16 patients had secondary infertility. Maximum patients (52) were seen in the age group of 25-30 years and more patients (50) were seen with marital life of less than 3 years.

The patients were called monthly and if no conception had occurred were asked to continue the treatment. Out of 88 patients put on treatment 62 patients conceived i.e. 70.45%. Pregnancy was confirmed by Elisa test initially and later by USG. The conception rates with regards to type of infertility, age, duration of marital life and duration of treatment is shown in Table I, II, III and IV respectively.

Infertility is a problem faced from time man has evolved and will probably remain with us for ever. Investigations of the cause of infertility in a systemic way is a very long

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TABLE I: CONCEPTION RATES OF PATIENTS ACCORDING TO TYPE OF INFERTILITY

TYPE OF INFERTILITY	NO. OF PATIENTS	NO. OF CONCEPTIONS	PERCENTAGE
Primary	72	55	76.39
Secondary	16	7	43.75

TABLE II: CONCEPTION RATES ACCORDING TO AGE DISTRIBUTION

TYPE OF INFERTILITY	NO. OF PATIENTS	NO. OF CONCEPTIONS	PERCENTAGE
<24 years	30	24	80
25-30 years	52	36	69.23
>31 years	6	2	33.33

TABLE III: CONCEPTION RATES ACCORDING TO DURATION OF MARITAL LIFE

DURATION OF MARITAL LIFE	NO. OF PATIENTS	NO. OF CONCEPTIONS	PERCENTAGE
<3 years	50	42	84
>3 years	38	20	52.83

TABLE IV: CONCEPTION RATES WITH RELATION TO DURATION OF TREATMENT

DURATION OF TREATMENT	NO. OF CONCEPTIONS	PERCENTAGE
2 months	13	20.96
3 months	23	37.10
4 months	26	41.94

procedure taking months to reach a conclusion. Even after all investigations including HSG, D&C, laproscopy with chromotubation, USG, hysteroscopy, in 30% cases, no causative factor can be isolated in either the male or female partner. Ultimately such couples have to resort to ART or adoption which can be depressing at times.

All the mentioned investigative procedures are time consuming and quite expensive which all the patients cannot bear. Patients with limited resources can be put on folic acid and vitamin B_6 therapy which has the advantage of being economical, safe with no side effects, out patient treatment, has easy administration, with no contraindications and having no surgical interference. Encouraging results have been obtained by Khushalani et al 2001,[5] in studying the efficacy of same drugs for treating infertility.

Conclusion

Treatment of infertility with a drug which is cheap, easily available without any side effects and showing good results should be accepted and tried on a larger scale.

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SOLITARY LARGE LUNG MASS AND AMENORRHEA IN A FEMALE SMOKER

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Abstract: *We describe a case of a large invasive lung mass in a heavy smoker. Although the mass resembled a primary lung cancer, it proved to be a metastatic choriocarcinoma. In absence of any previous molar pregnancy or abnormality on pelvic examination, pelvic ultrasound or CT scan, elevated levels of human chorionic gonadotropin (HCG) suggested a trophoblastic origin of the tumor. A large solitary invading mass is a rare presentation of metastatic choriocarcinoma.*

Key Words: *Lungs, Metastasis, Choriocarcinoma.*

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Report of a Case.

A forty two-year-old African-American female with 30-pack/year history of smoking presented with complaints of cough, hemoptysis and dyspnea on exertion of 1-week duration. The patient denied fever, chest pain or weight loss. She had delivered a normal fetus 11 months back and had ammenorrhea for 3 months. Physical examination revealed dullness of percussion and diminished breath sounds in the left upper chest. Examination of breasts, pelvis and rectum was normal. Chest x-ray (Fig 1A & Fig 1B) and CT scan of the lungs (Fig. 2) showed a 10 cm low density circumscribed mass extending from apical posterior segment of the left upper lobe to superior segment of the lower lobe, invading mediastinum, main and left pulmonary arteries and descending aorta. CT scan of the abdomen and pelvis and ultra sonography of the pelvis was normal. Serum beta HCG level was 8278 iu/ ul.. Transbronchial biopsy from left apico-posterior segment was consistent with choriocarcinoma, which stained positive for HCG. Subsequent endometrial curettage showed proliferative phase endometrium with fragments of decidua and trophoblastic cells. Further work up revealed evidence of metastasis to the right parietal culvarium, pelvic rami and cerebellum.

Patient was treated with chemotherapy and the regimen included methotrexate, VP16, cisplatin and bleomycin. Her clinical course was complicated by development of lung abscess and tubulointerstitial nephritis. The persistent lung mass was resected 6 months later and revealed presence of necrosis, chronic inflammation and fibrosis. A bone scan done 11 months after initial presentation showed absence of any metastatic lesions. One month later patient was admitted to hospital with sever shortness of breath and was found to have pneumonia in addition to bleomycin induced pulmonary fibrosis. She was discharged after therapy but did not return for further follow up.

Comment.

A large invasive lung mass in a heavy smoker raises a high suspicion of primary lung malignancy. However a trans-bronchial biopsy and elevated HCG level led to the diagnosis of choriocarcinoma. A possibility of metastatic origin of the mass was not considered initially since our patient had no previous history of molar pregnancy and pelvic examination and abdominal and pelvic CT scan did not show any abnormality. However, primary choriocarcinoma of the lung is an extremely rare form of extragonadal choriocarcinoma and it must be diagnosed only after an extensive search for the source of the tumor from gestational or gonadal origin has failed (1). Subsequent endometrial curettage in our patient revealed the source of metastatic choriocarcinoma.

Gestational choriocarcinoma is relatively uncommon and most patients with metastatic pulmonary choriocarcinoma have preceding molar pregnancy (2,3). Metastasis to lungs from trophoblastic tumors is common with a prevalence of 45-87% (3-6). Pulmonary metastasis usually presents in one of the three forms: 1)typical metastasis, 2) alveolar metastasis and 3) endarterial embolic form . Majority of the patients present with bilateral well defined multiple rounded nodules. These lesions are usually 1-3 cm large and are similar to metastatic lesions from other primary malignancies. Libshitz et al reported &

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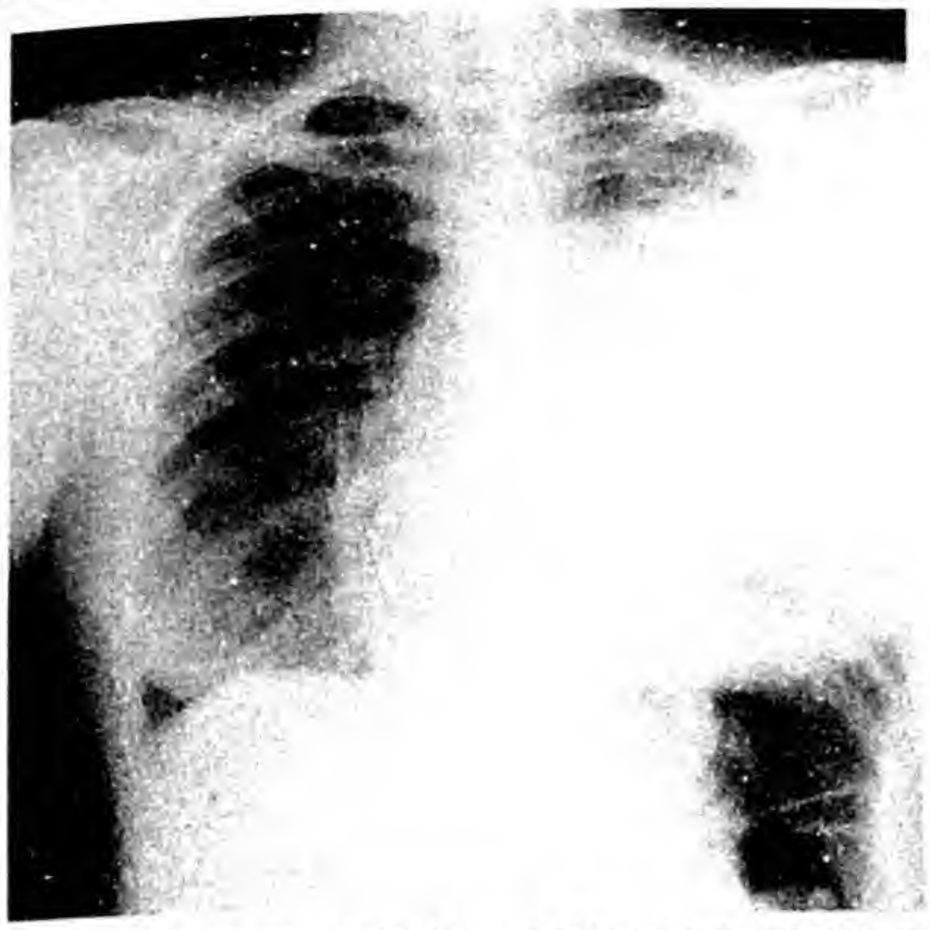

Figure 1A: Posterioanterior radiograph of the chest showing large circumscribed mass in the lung.

Figure IB: Lateral chest radiograph showing large circumscribed mass.

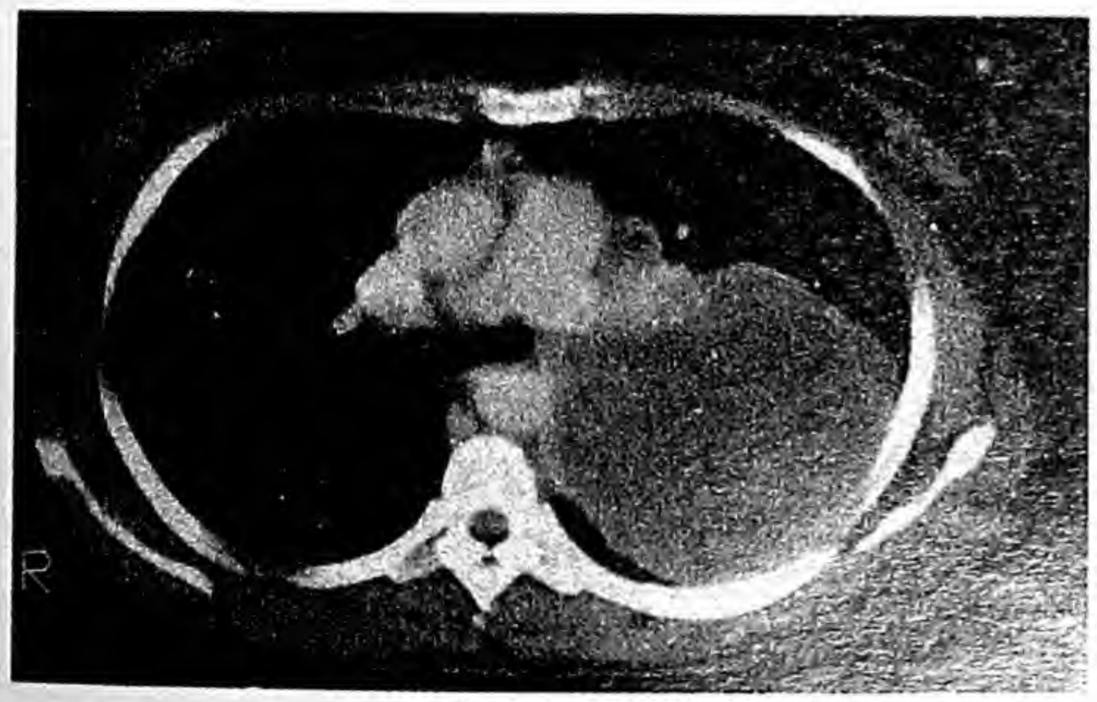

Figure 2: CT scan of the chest showing large lobulated mass on the left side extending to Mediastinum

multiple nodular pulmonary lesions in 94% patients with trophoblastic tumors who had metastasis to lungs[4]. Similar findings were reported by Bagashawe and Noble[5]. Occasionally these lesions may cavitate[6].

The next common type of pulmonary involvement is in the form of alveolar metastases and these appear as multiple small opacities with fluffy outlines scattered throughout the lungs or larger lesions resembling inflammatory processes. Bagashawe and Noble found 17% metastases of this type, while only 2 of 35 cases in the series reported by Libshitz et al had similar type of lesions. It has been suggested that hemorrhage around nodules or treatment with methotrexate may in part be responsible for the unusual appearance of these metastases[4].

Endarterial embolic form is a relatively less common form of pulmonary metastasis due to trophoblastic tumors and may present as pulmonary infarcts, indistinguishable from thromboembolic disease. Evans et al, reported pulmonary infarcts secondary to intra-arterial deposition of metastasis in 5 of 45 (11%) cases. This type of metastasis may not be evident radiologically unless the emboli are sufficient in number to cause pulmonary hypertension with secondary cardiovascular changes[3,4].

Solitary large pulmonary metastatic lesions are rare. Noteworthy feature in our case include a large solitary pulmonary mass infiltrating the mediastinum and large vessels at presentation mimicking a primary pulmonary malignancy. Amenorrhea and high HCG level raised a possibility of metastatic origin of the mass. Under appropriate clinical settings a high HCG level may be a valuable initial aide in the clinical diagnosis of metastatic choriocarcinoma. An extensive search for primary source of the trophoblastic tumors, including diagnostic uterine curettage should be considered even in presence of normal pelvic examination and negative radiography.

Generally patients with low risk choriocarcinoma have a good prognosis and mortality is lowest when diagnosed within 6 weeks of preceding pregnancy. The mortality increases progressively with increase in time interval between pregnancy and diagnosis and presence of metastasis on initial presentation. A malignancy discovered 7weeks to 3 months after pregnancy caries a mortality of about 55% which increases further to 75% if diagnosis is made 7 months to 5 years after pregnancy. Compared to molar pregnancy a choriocarcinoma following a normal pregnancy is considered as high risk, requiring aggressive chemotherapy with an over all mortality of about 15%[8]. In presence of poor response to chemotherapy surgical resection of solitary pulmonary lesion may be considered in patient who have no lesions elsewhere[3].

Our patient had multiple poor prognostic features ; the tumour was diagnosed 11 months after a normal pregnancy, and she had pulmonary, bone and cerebellar

metastasis at the time of presentation. Although tumour responded to the chemotherapy her clinical course was complicated by infections and complications secondary to chemotherapy.

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STRESS FRACTURE FOLLOWING RESECTION OF DISTAL END OF CLAVICLE

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ABSTRACT: *A stress fracture results from the mechanical fatigue of bone when it is subject to repetitive loading, such as in healthy athletes and military recruits, when its structural strength is compromised as in osteoporosis and the chronic administration of steroids and when changes in its mechanical axis lead to maladaptation of stress with osteoclastic supervening the osteoblastic activity. We report a rare case of stress fracture of the clavicle, following excision of its distal end for primary osteoarthritis of the acromioclavicular joint.*

KEY WORDS: *Stress fracture, Clavicle, Resection.*

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Introduction

Stress fractures are relatively frequent in weight bearing joints, less frequent in upper extremities, and rare in the clavicle[1]. Stress fractures of the medial portion of the clavicle have been reported in patients following radical neck dissection with subsequent muscular imbalance-"The pseudotumour"[2,3]. Cases have also been reported in academic pursuits, in patients with nervous ticks and following sport activities[4,5,6]. To our knowledge stress fracture of the clavicle following resection of its distal end has not been previously described.

Case report

A fifty two-year-old, right-hand-dominant self employed wall painter, presented with a painful lump over his left clavicle, which he developed while pushing a box of approximately 10 Kgs weight with his arm in above shoulder position.

The patient had history of excision of the distal end of clavicle for osteoarthritis of acromioclavicular joint, 18 months ago.

On examination there was a tender swelling over the middle third of his clavicle and shoulder movements were restricted because of pain. X-ray of the left shoulder revealed previously excised distal end of clavicle with a fracture of the middle third. (Figure1)

He was treated successfully in a broad arm sling.

Clinical follow up and x-ray at eight weeks revealed healing of fracture with excessive callus formation. (Figure 2.) At fourteenth week he returned to his work with fully healed and consolidated fracture (Figure 3), and when reviewed at two years he had pain free full range of shoulder movements. Anterior flexion power was found slightly decreased.

Discussion

A stress fracture most commonly occurs when excessive repetitive stress is applied to a bone. Bone is a dynamic tissue and in response to stress it strengthens and remodels. If bone does not have the structural strength to withstand stress, or maladaptation to stress causes osteoclastic activity to supervene osteoblastic activity, the bone eventually fatigues and breaks[7]. It has also been shown that muscle fatigue may increase strain on the bone, thus making the bone susceptible to rapid failure[8].

The present case report refers to a 52 years old male, who sustained a stress fracture at the outer part of the middle third of his left clavicle following resection of its distal end for osteoarthritis of the acromioclavicular joint. It is known that clavicle has several important functions, each of which can be expected to alter not only after excision of the bone but also following fracture, non-union or malunion. It is stated that the most important function of the clavicle may be its contribution to shoulder motion, which is related to its curvature, especially the lateral[9,10]. During combined glenohumeral, acromioclavicular, and sternoclavicular movement, the humerus moves about 120° at the glenohumeral joint and the scapula moves along the chest wall about 60°. Of the total 60° of scapular rotation, the first 30° are related to elevation of the clavicle as a whole by movement of the sternoclavicular joint, whereas the next 30° are permitted through the acromioclavicular joint by clavicular rotation and elongation of the coracoclavicular ligaments[9]. De Palma suggested that

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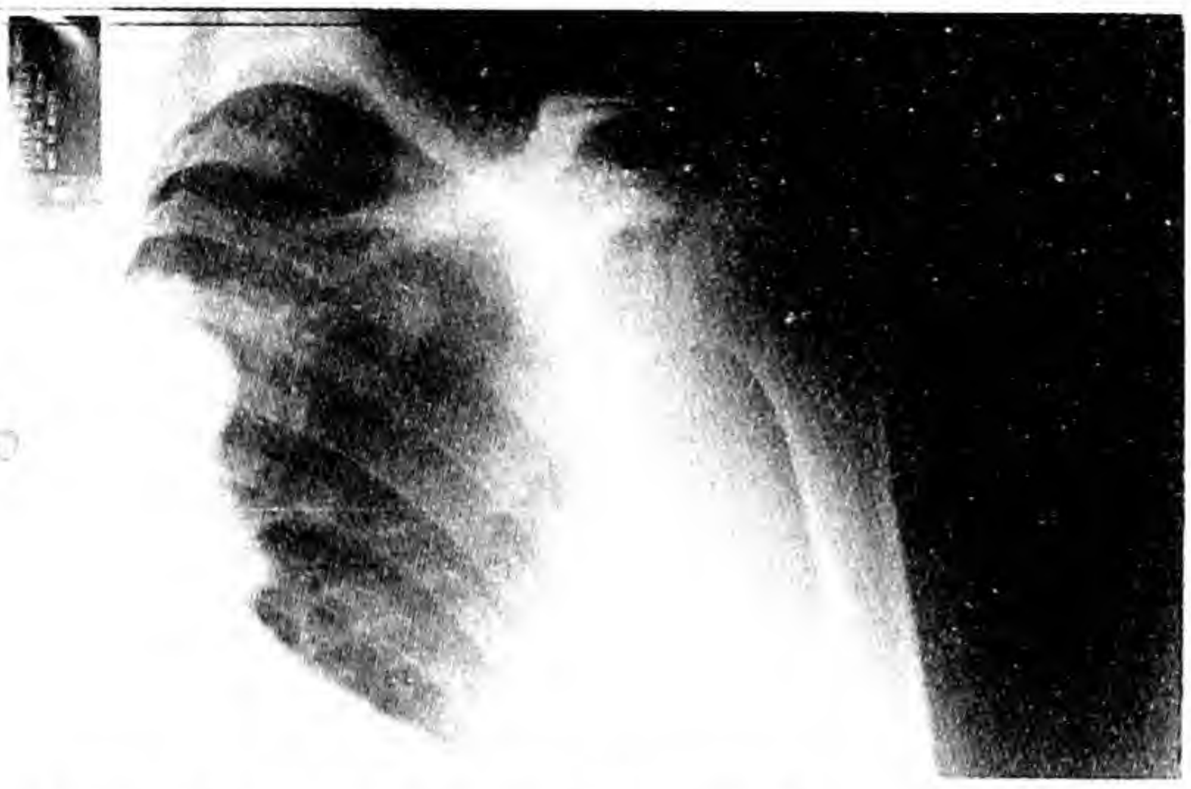

Figure 1. Initial radiograph showing excised distal end of clavicle with stress fracture at middle third.

Figure 2. Radiograph at 8 weeks, showing uniting fracture with callus formation.

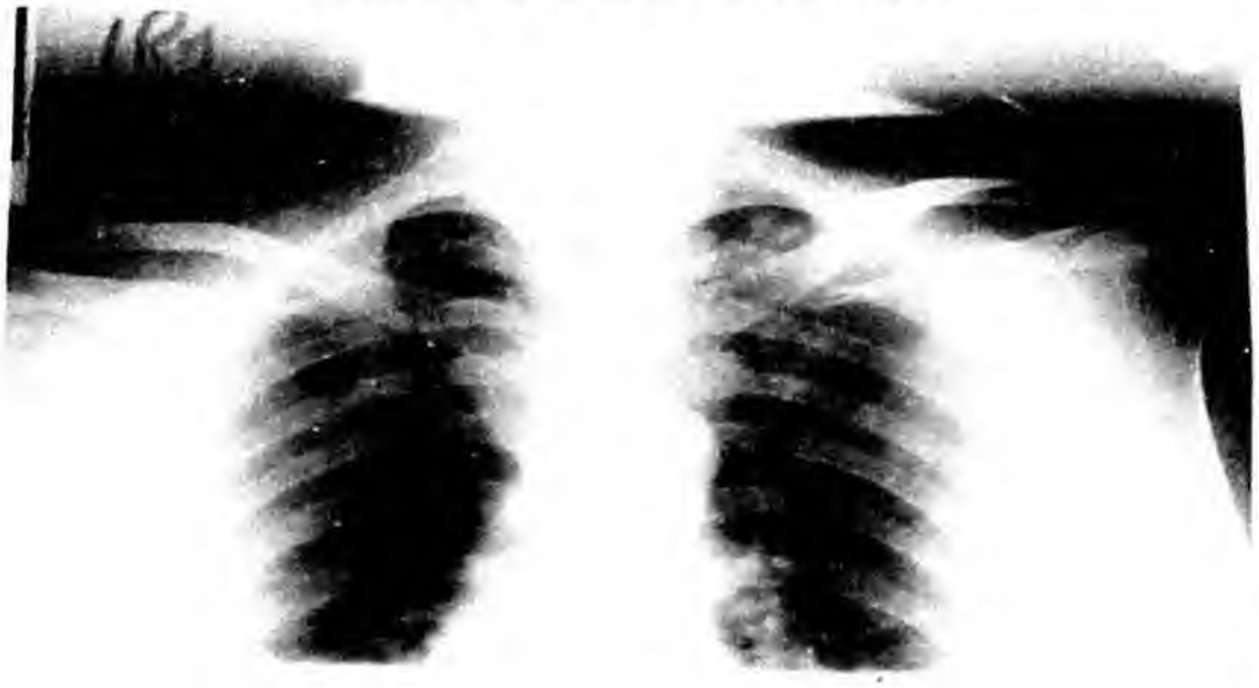

Figure 3. Radiograph at 14 weeks showing well healed and consolidated fracture.

changes in torsion might alter stresses and lead to primary degenerative disease in the acromioclavicular joint[11]. However he did not specify whether these torsional forces continue to exist or even increase after resection of the distal end of the clavicle leading to stress fracture as in this case.

Resection of the lateral end of the clavicle, frequently performed for persistent acromioclavicular joint pain, disrupts the acromioclavicular articulation and creates the potential for abnormal postoperative motion[12,13]. It has been shown that the total translation of the clavicle in the anteroposterior plane after excision of its distal end was 8.7mm(range, 3-21mm), being significantly greater than that of the contralateral normal side (mean 3.2mm, range 1-6mm)[14]. This abnormal postoperative motion and translation may give raise to additional forces on to the bone and lead to stress fracture as in our patient.

The cross section of the clavicle differs in shape along its length, varying from flat along the outer third to tubular along the middle third and prismatic along the inner third. The flat outer third is most compatible with pull from muscles and ligaments, whereas the tubular middle third is compatible with axial pressure or pull[9]. The junction between the two cross-sections varies in its precise location with the middle third of the clavicle, being a weak spot[15]. In addition, this area is not reinforced by muscles and ligaments, is just distal to subclavious muscle insertion and is the thinnest part of the bone, which makes it susceptible to fracture[16,17].

Conclusions

Contribution of clavicle by means of inferosuperior, anteroposterior, and rotational motion during shoulder movements is known and is exacerbated in above shoulder level use of the arm, especially after resection of its distal end, which results in additional stresses producing fracture.

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ISOLATED CORROSIVE INJURY TO STOMACH FOLLOWING ACCIDENTAL ACID INGESTION

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ABSTRACT: Injury to UGI tract due to ingestion of acidic corrosive substances is common in India. Knowledge of spectrum of injury due to acid ingestion is scant owing to the fact that acid intake accounts for mere 5% of all the reported cases. Isolated injury to esophagus or stomach though uncommon have been reported in literature. We report a case of isolated injury to stomach following accidental acid ingestion.

KEYWORDS: corrosive injury, acid corrosive injury, spectrum of injury.

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INTRODUCTION.

Ingestion of corrosive substances have devastating effects on the upper GIT and present major problems in management.[1]

Ingestion of corrosive substances either accidentally by children and alcoholics or intentionally for purpose of suicide is a common form of poisoning in India.[2,3] Where as contiguous injury to the esophagus and stomach are common following alkali ingestion[3],the isolated injury to the stomach following acid ingestion though rare are reported[2].

CASE REPORT

A 35 year old male alcoholic goldsmith with 15 days prior history of accidental ingestion of "aqua regia" (HNO_3:HCL,3:1) presented to the surgical emergency with h/o gastric outlet obstruction. There was no h/o prior medical treatment. Prior h/o pain epigastrium was present.

On examination the patient was dehydrated and emaciated with B.P of 90/60 mmHg and pulse rate of 100/ min. There was no respiratory distress or subcutaneous emphysema. Patient was pale and afebrile. Examination of chest was unremarkable. Per abdomen examination showed mild tenderness in epigastrium.

Routine investigations showed hemoglobin of 8 gm% and slightly raised counts(12500). CXR and AXR were normal.

ENDOSCOPY Showed decreased distensibility of esophagus with open LES. No hyperemia/ulcers/stricture was seen in esophagus. Stomach showed greatly reduced capacity with hyperemia and ulcers in fundus and body . Distal stomach was severely narrowed with endoscope not negotiable.

BARIUM MEAL Showed normal esophagus with gastroesophageal reflux. Stomach showed decreased distensibility and capacity with ulcers in fundus and body. Distal stomach was narrowed with only a string of barium passing to duodenum. Duodenum was normal.

Assessment and feeding juejunostomy was done under GA via midline incision. Intra op assessment showed grossly inflamed stomach. Distal stomach was thickened and narrowed. No area of full thickness burned identified. Feeding was started via feeding juejunostomy and patient followed up every two weeks. Three months later when the nutritional status improve, patient planned for total gastrectomy and Roux-en-Y reconstruction. Pre op Barium meal showed essentialy normal esophagus with stricture antropyloric region. Proximal stomach showed mucosal irregularity with decreased capacity and distensibility. Intra op findings showed severely narrowed and thickened distal stomach with normal appearing proximal stomach. Duodenum was normal. Billroth type 1 gastrectomy was done. Post op recovery was uneventful with patient discharged on 10th post op day. Post op Barium meal showed irregular stomach mucosa with normal flow of barium from remnant to the duodenum.

Patient is still under follow-up and doing well.

DISCUSSION

Ingestion of corrosive substances either accidentally or intentionally for the purpose of suicide is a common form of poisoning in India[3].Unlike in the west, accidental or suicidal ingestion of acids is common type of poisoning in India because of easy access to acids as they are used as cheap toilet cleansers[2].

As the acid intake accounts for only 5% of all reported

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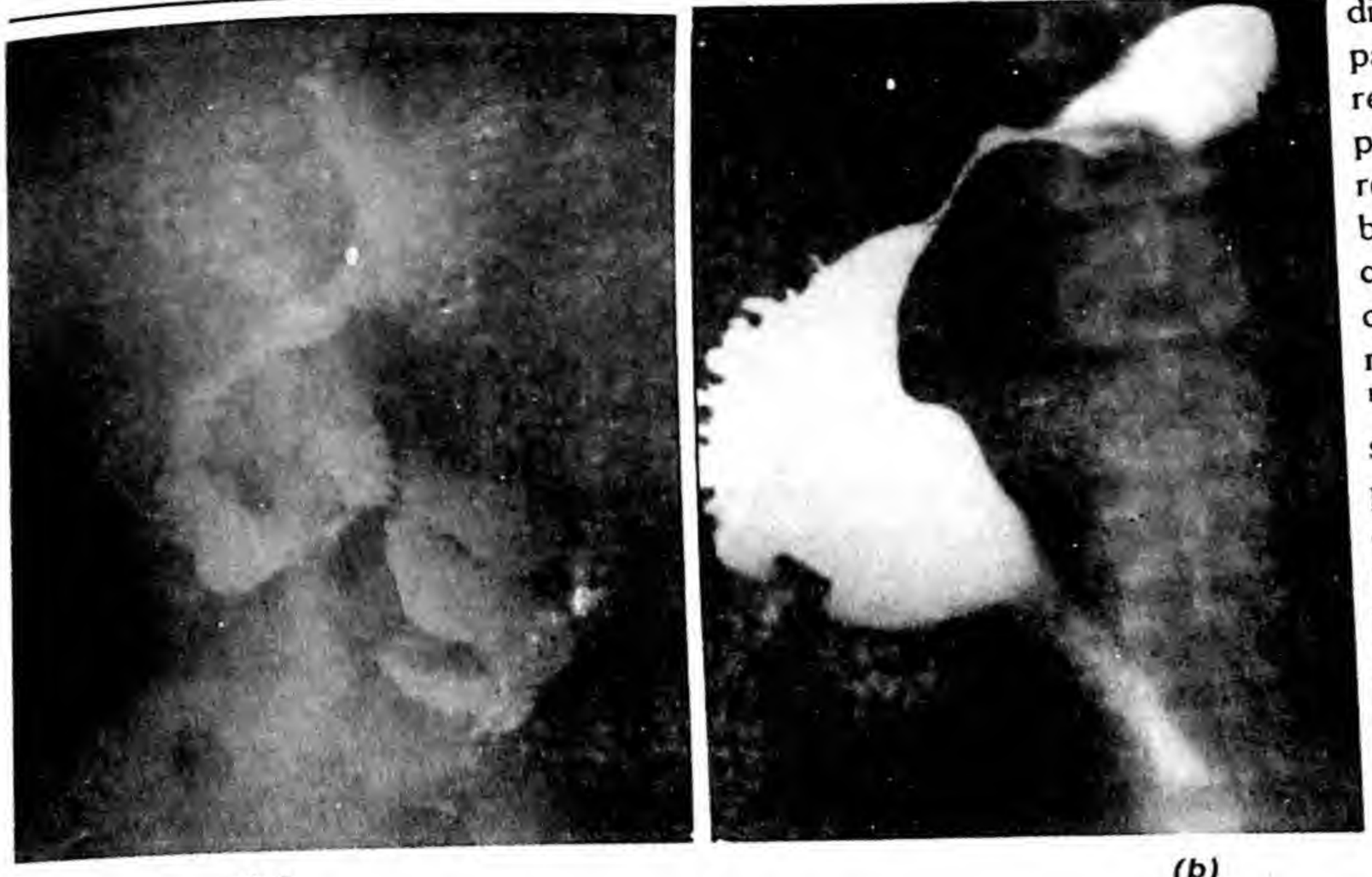

(a) (b)

Barium Meal: Accidental Acid Ingestion. (a) Preoperative (b) post operative

cases in west, the knowledge of the spectrum of injury to UGI tract due to corrosive acidic substances is scanty[2]. Individual case studies[4-6] or studies of small number of cases[7,8]) have led to the suggestion[6-10]) that acids cause maximal damage to the stomach and relatively minor damage to the esophagus because of rapid transit and the great resistance of squamous epithelium to acids. But a study by Zargar et al[2] from India have shown different results. They prospectively evaluated 41 patients who ingested acid for location,extent,severity and outcome of the injury to UGI tract. The injury was assessed within 36 hours of acid intake by endoscopy or surgery or at autopsy. Esophageal injury was seen in 87.5% of cases, gastric injury in 85.4% and duodenal injury in 34.1% of cases. The esophageal and stomach was damaged in 80.5%of cases with associated duodenal injury in 34.1%of cases. Isolated involvement of esophagus and duodenum was present in 3 and 2 patients respectively. They found that signs and symptoms are unreliable in predicting the extent and severity of injury. Also endoscopy is not only the tool of choice for diagnosis but also aids in deciding upon treatment and prognosis. They concluded that acid injury of UGI tract is a serious condition that effects esophagus and stomach equally and results in high mortality and morbidity.

Ingestion of corrosive substances have devastating effects on UGI tract. Immediate management should be directed at securing an airway,relieving pain and attending to intravenous fluid replacement. Patients with signs of perforation should undergo immediate resection[1]. Flexible endoscopy should be carried out as soon as the patient's condition stablises to grade the severity of injury and to minimize delay in recognizing full thickness injury [1,2,3]. Patients with full thickness burns should undergo resection whereas patients with mild to moderate burns can be managed conservatively. Patients beyond 2nd degree burns should be given parenteral antibiotics. Long term follow-up is required to treat the late complications[1].

Isolated injury to stomach can be explained on the basis of (1)Relative resistance of squamous epithelium to acids.(2) Rapid transit through esophagus (3) Reservoir function of stomach allowing accumulation of large volume of acid in stomach (4) Reflex pylorospasm increasing the contact time between the acid and the stomach mucosa..

So isolated acid corrosive injury to stomach though rare has been reported in literature.

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HYDATIDOSIS: RARE PRESENTATIONS

Anjum Fazili M.S.; Nazir Ahmed Wani M.S.; Tahir Saleem Khan M.B.; Abdul Rehman Mir M.S.

Abstract: *Hydatid disease is a common entity in this part of the world because of the fact that this is a zoonotic illness and sheep rearing and its use is very high in our state of J&K. Hydatid cyst, which is caused by an eccinococcus infestation, has a very diverse presentation. It is relatively common in sheep rearing areas like Australia, South America, Iran, Iraq; Greece while highest incidence is seen in British Isles and Wales. The disease has an endemic course in Asia. Apart fronm involving liver (75%) and lung (15%) as its most common primary target organs, it has a property of involving any part of the body. We present two such rare cases of hydatid cysts encountered in our surgical practice, where the cyst was lodged at the most unusual site.*

Key words: *Cyst, Eccinococcus, hydatid*

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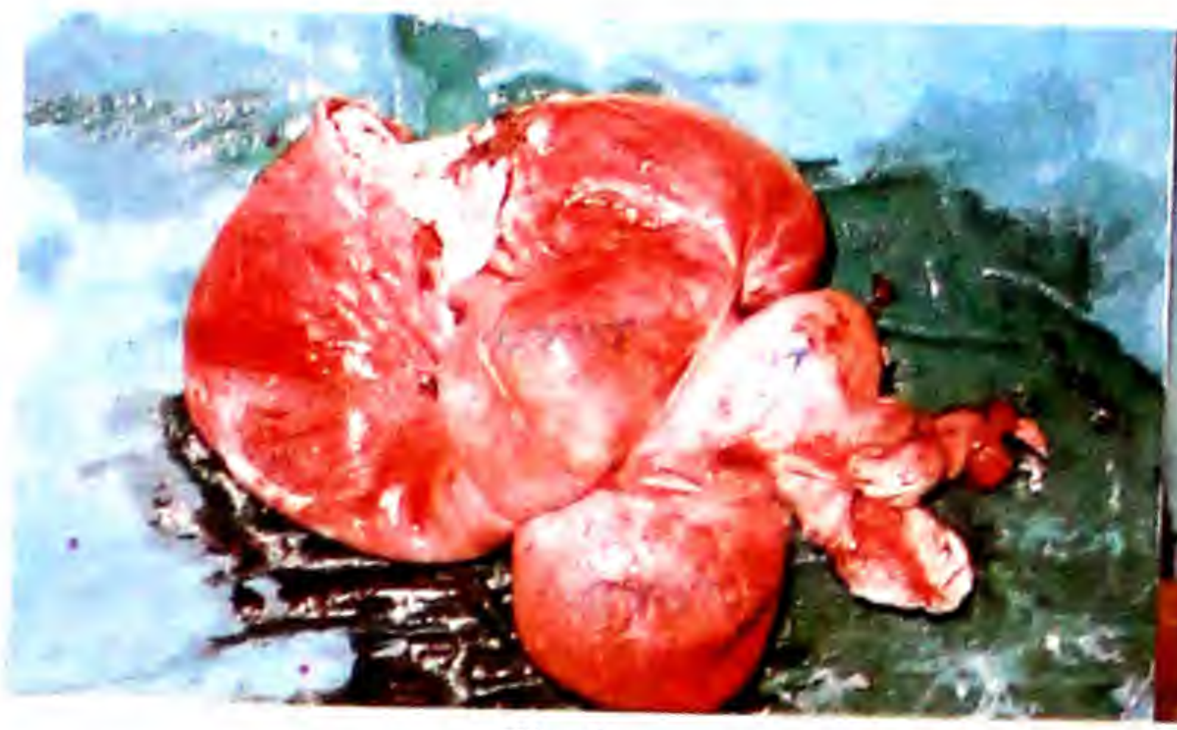

Fig.I.

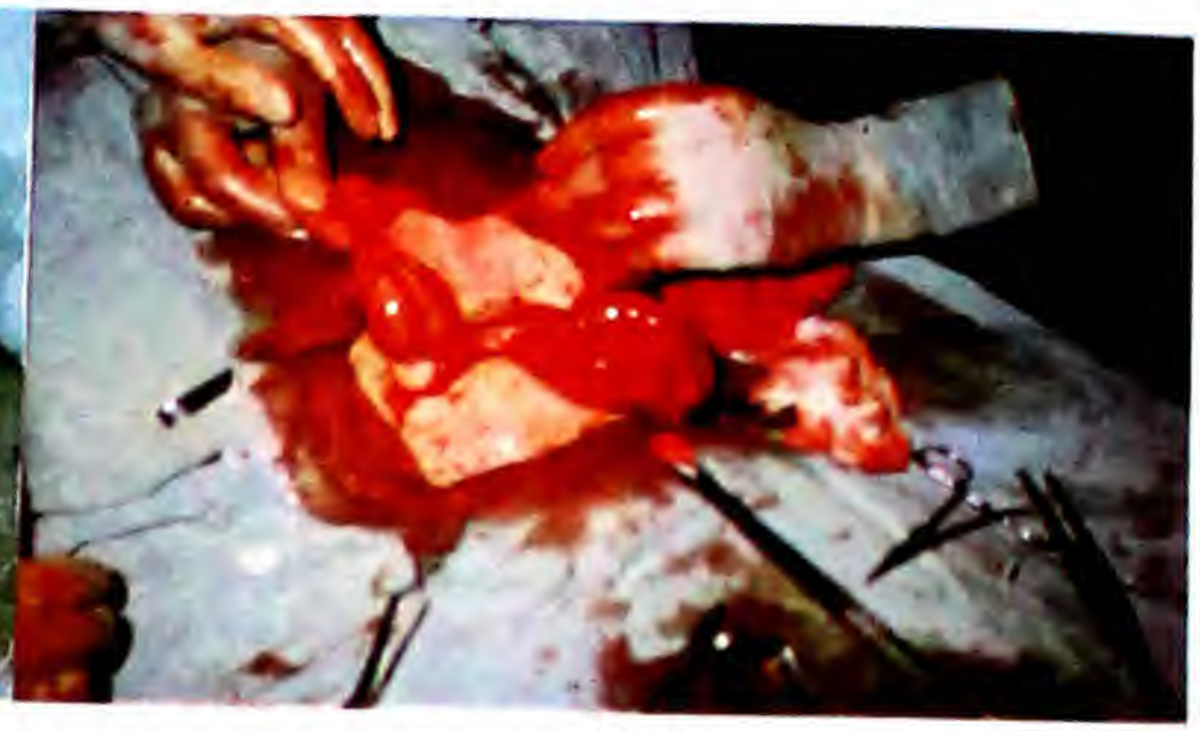

Fig.II.

Case I (Figure 1):

A 45 year old female multigravida with a completed family bearing three children, two daughters and a son, from district Kupwara was shifted from Lal Ded hospital Srinagar as a case of peritonitis due to rupture of a suspected ovarian cyst. Patient was routinely investigated, ultra sonogram showed a cystic swelling possibly arising from right adnexia. Paracentesis done was positive revealing some straw colored fluid. Patient was operated which revealed two unruptured cystic swellings, one arising from posterior wall of uterus and another from vault of uterus. Both ovaries were found to be normal but adherent to the cystic swellings. Taking into view the nature of the disease, fixed cystic swellings, an on table decision for total abdominal hysterectomy was taken. The cystic swelling was opened and hydatid-laminating membrane was found and was also confirmed histologically.

Case II (figure 2):

A 12 year old female child was admitted in our ward as case of cystic swelling abdomen, which was moving in all its quadrants. A provisional diagnosis of a simple mesenteric cyst was made and the patient was routinely operated which revealed a hydatid cyst of the mesentery of small gut. Hydatid cystectomy was performed sparing any damage to the gut wall. The cyst was unilocular and diagnosis was also confirmed histologically. Patient was discharged on 10th postoperative day when all sutures were removed. patient behaved normally during her follow up. Mesenteric hydatid is so far unreported in the literature. The operative photograph of the same is shown as figure no 2nd.

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Discussion:

Liver and lung are the most common organs involved in hydatid disease and it has a property to involve any blood fed organ. Various studies have given their experience regarding the rare presentation of the hydatid. Peritoneal hydatidosis has been seen in 6.9% cases and it is usually attributed to rupture of previous hydatid liver or spleen[1]. In another vast study of 74 cases of hydatidosis, only two patients had extra hepatic hydatid (one in spleen and one in spleen & lungs)[2]. Yet another rare presentation seen has been in the pancreas[3,4], and another in diaphragm[4]. Uterine hydatid is a rare presentation and has been seen in literature[5,6,7]. In one study uterine hydatid has been seen to cause obstructed labour[8].

Mesenteric hydatid is the most unreported site so far as literature goes. In our case report a young female child had hydatid cyst in the mesentery and there was no history of any previous hydatid disease in her.

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ECHINOCOCCAL DISEASE OF THE KIDNEY PRESENTING AS RENAL FILLING DEFECT

Rahul Gupta M.S.; Imtiaz Shah M.S.; CL Gupta M.S.

Abstract: *We report a unique case of renal echinococcal disease. The patient presented with left poorly functioning kidney with calcification, without hepatic or pulmonary involvement. Management consisted of successful exploration and left nephtectomy.*

Key words: *echinococcus, kidney, nephrectomy.*

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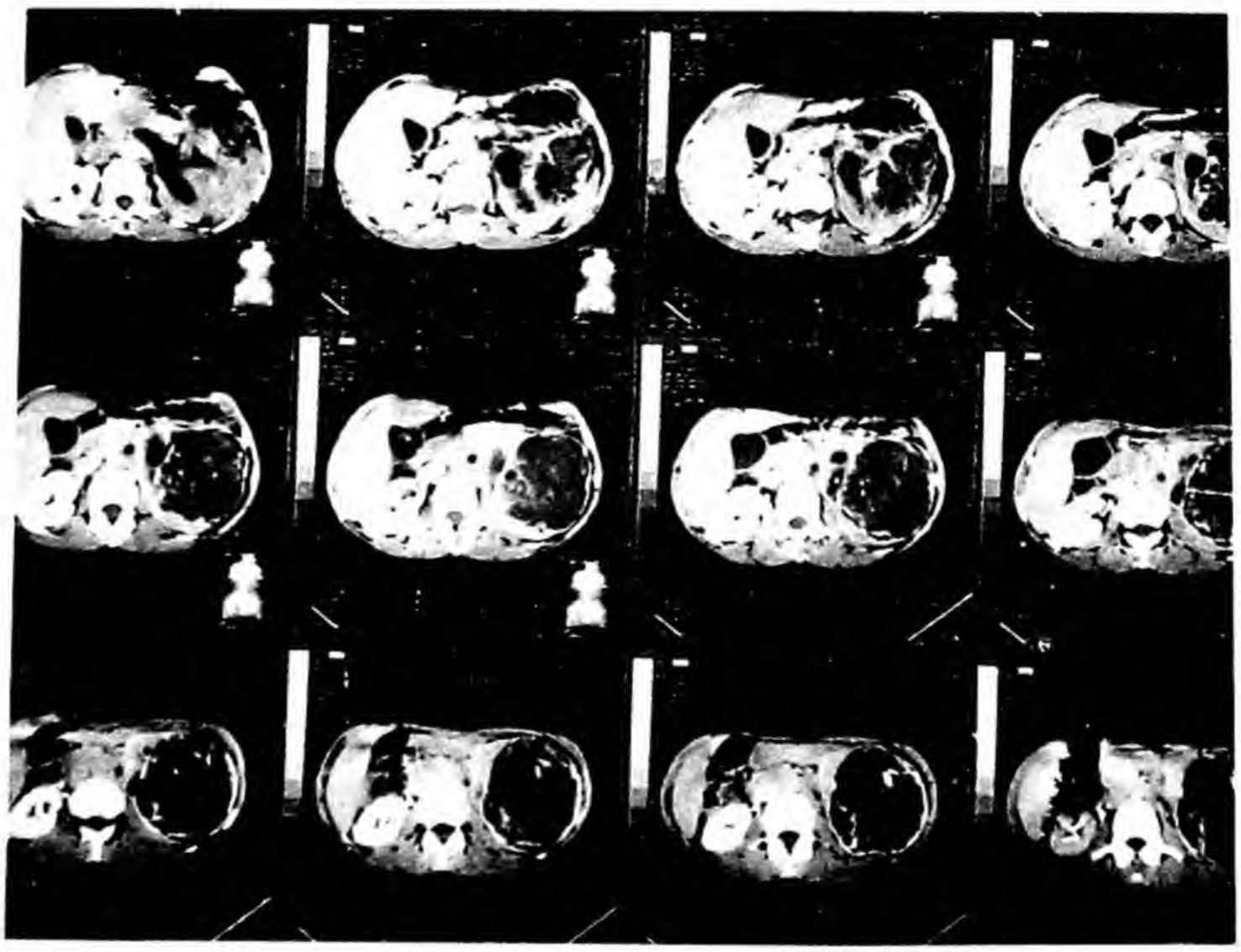
Introduction

Renal involvement of hydatid disease is rare, comprising only 2 to 3 per cent of all cases[1]. Hydatid disease is endemic in certain areas of Australia, Asia, and Europe[2]. Man is an intermediate host in echinococcus granulosus infection and since there is no safe systemic agents available to treat this disease surgical intervention is necessary to remedy the renal involvement.

Case Report

Thirty eight years old female presented with history of dull aching pain in the left flank with painless intermittent heamturia for last six months. Clinically the left kidney was palpable and ballotable with firm in consistency. Complete blood count and renal parameters were within normal limits, routine urine microscopy revealed puss cells and RBC, plain x-ray of abdomen showed a well defined rounded calcified rim in the left renal area and intravenous pyelography confirmed the poorly functioning left kidney with normal functioning kidney on right side. Dynamic CT scan abdomen showed left renal mass measuring 14.5x6.7 cms with faintly visualized septates within it and thick enhanced capsule, with poor excretion of dye. Patient was diagnosed as left renal mass and was subjected to surgery for left nephrectomy through transperitoneal approach. Per operative there was a mass involving the lower pole with perirenal adhesions. Cut sections of the mass surprisingly revealed mixture of blood clots and lamelle and hooklets, tentative diagnosis of echinococcus granulosus was made which got confirmed pathologically in post operative period.



Discussion

Hydatid disease is an infection of various organs by tapeworm Echinococcus granulosus. Hippocrates were

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familiar with hydatid cyst but it was not until 1782 when Goeze discovered the relation ship of the scolices to the formation of cyst. The dog being the primary host, the eggs are excreted in feaces these eggs are taken up by intermediate host such as man, sheep and other animals. In man ova hatch and the larva are absorbed through intestinal wall, after passing the first filter i.e. liver or second filter i.e. lungs, larva seed and form a reactive cyst in the end organ. It may take 15-20 years to reach to its pathological size. Genitourinary involvement is almost uniformly renal in origin, but prostatic, bladder and epididymal involvement has been reported. Presenting complaints are typically of flank mass, heamturia and pain[3], occasionally as a result of rupture of the cyst into collecting system the patient pass typical "grape" like material in the urine.[4] Casonis skin test, the comlement fixation serological test and heamagglutination test which offer low reliability of 80-85%[5]. Safe puncture of cyst for sampling also has been reported.[3]

The surgical approach to a hydatid cyst is easiest and safest. The skin incision should always be placed in such a manner as to expose the part of cyst directly. Echinococcal disease of the kidney is treated either by nephrectomy or evacuation of the parasite[5], depending upon the functional capability of kidney and exposure should be extraperitoneal and spillage of cyst contents should be avoided using scolicidal agents like formalin, hypertonic saline, hydrogen peroxide, alcohol which reduce the risk of seeding and anaphylasis. Post operative antibiotics are indicated for bacterial super infection.

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MARFAN'S SYNDROME WITH INFECTIVE ENDOCARDITIS & INTRACEREBRAL HEMORRHAGE

Majid A. MD; Khan M.A. MD; Shah P.A. DM; Bhat M.Y MD; Lanker S.S. M.B.B.S.

Abstract: *Marfans syndrome is complicated by cardiovascular abnormalities which can be further complicated by IE. IE is attended by a large No. of complications including neurological ones. However stroke due to intracerebral hemorrhage is quite uncommonly seen. Its incidence is 5% of stroke in IE.*

Key words; *Marfans syndrome, infective endocarditis, stroke.*

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A tall statured 16yr old boy was brought with history of grade fever, dyspnoea and palpitations of 25 days duration. Nothing was suggestive of rheumatic fever, chest trauma, collagen vascular disease, any surgical intervention or IV drug abuse.

GPE revealed marfanoid features - tall stature with lower segment > upper segment and arm span > total body height, arachnodactyli, high arched palate, positive thumb (Sternberg), & wrist (Murdoch) signs. Other positive findings were pedal edema & most of peripheral signs of aortic regurgitation.

System examinatin revealed hepatomegaly & murmur of MR (4/6 grade), & AR (3/6 grade).

Investigations:

CBC-Hb 9mg%, neutrophillic leucocytosis, increased ESR

Urine - microscopic hematuria

CXR-Cardiomegaly of left ventricular type & prominent upper lobe vessels

ECG - sinus tachycardia, high voltage R waves in V5, V6.

ECHO-MVD with predominant MR. Aortic valve disease with predominant AR, with multiple vegetations on both surfaces of anterior mitral leaflet. No thrombus & no mitral stenosis.

Blood culture- No growth of microbes.

Considering clinical and lab findings, diagnosis of Marfans syndrome with MR & AR with IE & CCF was made & patient was managed with salt restriction, bed rest diuretics and empirical antibiotic regimen of benzyl penicillin and Gentamycin.

On third day of hospital stay patient became drowsy & physical examination revealed left hemiplegia without signs of meningeal irritation. C.T. Brain was ordered which showed ICH in parietal lobe with midline shift. Patient was managed for stroke besides continuation of treatment for IE.

Discussion:

Marfans syndrome is an autosomal dominant syndrome with a prevalence of 1 in 1 lac population, occurs in all ethnic groups, may be familial or due to new mutation (30%), is due to mutation in fibrillin gene on long arm of chromosome 15. The diagnosis of Marfans syndrome with classical phenotype remains largely clinical. The three systems commonly involved are the Eye, the skeletal system & cardiovascular system. The most common cardiovascular features are MVP & dilatations of sinuses of valsalva. Children tend to be more severely affected by mitral valve disease whereas aortic problems are progressive and more likely in adolescence and beyond.

The patient under discussion had both mitral regurgitation and aortic regurgitation and was complicated by infective endocarditis on mitral valve.

IE is attended by a number iof complications among which neurological ones occur in 30-40%. Neurological complciations include - Encephalopathy (due to multiple micro-emboli) -10% Meningitis 5%, brain abscess 51%; Stroke; TIA; Peripheral neuropathy; seizures; unruptured mycotic aneurysms (potential clue is severe headache). Mycotic aneurysms with or without rupture occur in 2-10% of patients wth IE and approximately half of these occur in intracranial arteries.

Stroke in IE may be embolic or hemorrhagic. Embolic stroke is the most common variety-20%, intracranial hemorrhage occurs in 5% of patients with IE. In our case patient had hemorrhagic stroke. ICH in IE can result from

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(i) rupture of mycotic aneurysm (ii) rupture of an artery due to septic arteritis at the site of embolic occlusion. (iii) Hemorrhage into infarct. (iv) Anticoagulants for mechanical prosthetic valves. (v) IV drug abuse e.g. cocaine.

In our case ICH was most probably due to septic arteritis as there was no preceding headache which could suggest mycotic aneurysm, nor did CT brain show any signs of an infarct and obviously patient was not on anticoagulants and had no history of IV drug abuse.

This was a case of Marfans syndrome with IE with ICH-an uncommon presentation.

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DIABETES IN ELDERLY PATIENTS

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Definition:

DIABETES MELLITUS is a syndrome characterised by chronic hyperglycemia and disturbances of carbohydrate fat and protein metabolism, associated with an absolute or relative deficiency in insulin secretion and/or insulin action.

Prevalence:

Elderly people are those who are aged more than 65 years. Between 65-69 years it is an OLD; between 70-79 years it is an OLD OLD; and more than 80 years it is an elderly Old. Because of the better health care facitlities for all by 2000, the numbers of elderly persons is increasing and now constitute a good proportion of the general population. According to one estimate the elderly people consititute 8.3% of general population. By 2002, the figure of the elderly people in India is about 75 million.

There are about 3.5 crore diabetics in India and the figure will rise to about 5.2 crores by 2025. Every 5th patient visiting a consulting physician is a diabetic, and, every 7th patient visiting a family physician is a diabetic. Keeping in view the alarming increase in the incidence and prevalence of diabetics in India, WHO has declared India as the "**Diabetic Capital of the World".** More than half of diabetics (53%) are above 60 years and more than 85% are above 45 years. In India the prevalence of Diabetes is 11% between 65-69 years age.

Diagnostic Criteria:

American Diabetic Association uses FPG as a criteria of diagnosis, while WHO uses the Oral Glucose Tolerance test as parameter. As the FPG increases by 1-2mg/dl/decade and that of PPPG by 15 mg/dl/decade after 30 years of age, the WHO parameter overestimates the diabetes in elderly and the ADA criteria under diagnosis the diabetes in elderly. However for all practical purposes the ADA criteria of FPG in the diabetic range (≥126 mg./dl) means more of hyperglycemia.

Associated Problems Affecting Management in Elderly

1. Cerebral Aging : This disables an early diabetic with senile dementia and cognitive defects. It thus influences the management of diabetes mostly relating to diet, drug intake and personal hygiene

2. Atherosclerotic Changes: There occurs an isolated systolic hypertension due to anterosclerosis leading to an increased risk of stroke, renal failure, visual loss and cardiovascular events etc.

3. Compromised Cardio Respiratory Reserve : Decrease in it is a part of aging process leading to decrease in exercise endurance. Mild degree of discomfort leads to precipitation of cardiac events and more susceptibility to lower respiratory tract infections.

4. Blunting of Hormone Profile: This blunting especially includes the hormones of flight and fright (especially catecholamines and glucocorticoids). Any major assault destabilises the hemostasis and affects the management of disbetes and also leads to irreversible damage to various organs.

5. Poor Hepatic Glycogen Reserve: Elderly people, because of mal-nutrition, decreased appetite, etc., do not have sufficient glycogen reserves to mobilise. Insufficient release of adrenaline and glucocorticoids cause insufficient gluconeogenesis and lipolysis to form non-esterified fatty acids (NEFA). Blunted production of NEFA in stressful situations in elderly diabetic causes vital organ damage, especially of brain and heart.

6. Cataract : Age and DM both contribute to its causation. There may be an associated retinopathy, which may go undetected and may progress to the state when even cataract surgery does not give the desired benefit.

7. Neuropathy : In elderly the problems are mainly encountered due to autonomic neuropathy, and include postural hypotension, incomplete evacuation, diabetic diarrhoea, etc. Impaired proprioception makes them difficult to move. Neuropathy, atherosclerosis of peripheral vessels and poor vision makes them more likely to get diabetic foot problem. Neuropathy and atherosclerotic changes also contribute to sexual impotence in a reasonable number of elderly diabetics.

8. Cerebro Vascular Disease: Diabetes and age both contribute to cerebro-vascular accidents. In addition to causing paralytic strokes, it can cause vertebro-basilar insufficiency thereby causing multiple problems in daily living like vertigo, vomiting, tinnitus, diplopia etc.

9. NKHS and Hyponatremia: In elderly, because of associated dehydration, infection, surgery, etc., the electrolyte imbalances, especially, hyponatremia and NKHS

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are increased.

Management:

Tripod of Management = Diet
= Exercise
= Drugs

Minimum Standards of care for older Adults & DM:

This includes a) Initial Evaluation
b) Continuing Care

In the initial evaluation, the following parameters are taken into consideration:

- Complete history and physical examination
- Geriatic Assessment
- Laboratory Examination: Fasting Blood Glucose, Glycosylated Hemoglobin, Fasting lipid Profile, Creatinine, Urinalysis, Electrocardiogram
- Opthalmologic examination
- Dietary Assessment

In the continuing care the considerations are:

- Use of treatment as needed to meet target glucose levels: Diet, Oral agents or Insulin
- Assessment of blood glucose levels as frequently as needed
- Annual Assessment for Diabetes complications.
- Annual review of geriatic assessment.

A) Dietary Therapy:

Dietary therapy in elderly diabetics is a problem in itself, because of various co-existing features. Special consideration for older adults are:

- Financial difficulty
- Difficulty with shopping because of transportation or mobility problems.
- Poor food preparation skills (especially of elderly widowed men)
- Ingrained dietary habits.
- Difficulty following the dietary instructions because of impaired cognitive function.
- Decreased taste due to loss of taste buds.
- Increased frequency of constipation
- Problems with chewing because of loss of teeth,

Keeping in view all these consideration in elderly, quality, quantity and frequency, all have to be modified as per the person concerned. However, the total calories and its distrubution should more or less correspond to the standard dietary therapy.

B) Exercise:

Potential benefits and risks of exercise for older adults are:

Benefits	*Risks*
Improved exercise tolerance	Sudden cardiac death
Improved glucose tolerance	Foot and joint injuries
Improved maximum oxygen consumption	Hypoglycemia
Increased muscle strength	
Decreased blood pressure	
Decreased body fat	
Improved lipid profile	
Improved sense of well-being	

Because of co-existence of other ailments like osteoarthritis, Parkinsons disease, Visual impairment, Poor vital reserve, etc., exercises should be carried out in familiar surroundings and should be isotonic rather than isometric.

C) Drugs:

Basic principle of drug therapy is:

a. Hypoglycemia should be avoided
b. Tight control of glucose should not be attempted FPG should be maintained between 110-140 mg% and 2 Hr. PPPG should be maintained between 140-160 mg%. Inadequate intake, poor glycogen reserve, blunted catecholamines and adrenaline effect, all cause hypoglycemia.

Basic principle of therapy is decided by the state of hyperglycemia:

a. Mild Hyperglycemia : Insulin sensitizers are preferred
Drugs of choice are as follows
Obese - Metformin
Non-Obese - Troglitazone
Rosiglitazone
- Glimepride
- Acarbose

b. Moderate Hyperglycemia: Gliclazide is preferred
Long acting drugs should be avoided
Repaglinide is preferred in post Prandial state

c. Severe Hyperglucemia : Insulin has to be used
Regular insulin in small and frequent doses is ideal.
Supplementation of NPH Insulin to oral hypoglycemics should be avoided in elderly.

Insulin therapy in older adlults requires special considerations because of associated problems, which may under/over dose the person.

These problems include:

- Visual impairment
- Manual dexterity
- Sensation to hands (due to loss of touch 7 vibrations)
- Access to insertion sites
- Cognitive function
- Family support and
- Cost.

DIFFUSE ENDOCRINOLOGY THE (APUD- SYSTEM) ANATOMICAL, HISTOLOGICAL AND CLINICAL PERSPECTIVES

Ghulam Hassan MS; Mohd Shafi M.S.

Abstract:

Manifestations of certain neoplasms of the body is not always typical. They can prove intriguing to the clinician. Such neoplasms can be life consuming. At times these atypical presentations have been difficult to diagonose, and difficult to treat. Due to recent advances in radiology and Histopathology, detection of these previously rare entities have become common now adays.

The endocrine system is the most widespread and segregatted system in the human body classified as the Diffuse & the Classic Endocrine system. In The Diffuse System, the part receiving the prime focus is the APUD System, (Amine Precursor Uptake & Decarboxylation System) with the performance of specialized functions.

- Paracrine functions
- Endocrine functons
- Autocrine functions
- Circadian functions

Origin:

Pearse proposed the Unifying theory which postulates a common origin of the Apud System from Neural Crest.

Diffuse origin theory from multipotent stem cells and implantation at different sites, which is more widely accepted & in accordance with the wide distribution of the system.

Histology:

The Apud System is the most widespread in the Gut espically small intestine & a part of the large gut. There are about 28 cell types. The cells are designated as clear cells the name clear cells is given because of their special histological behaviour.

These cells don't have suff icent RNA to import Basophilia & nor sufficient membrane to import Acidophilia to the cells. The routine Haemtoxyline & Eosin stains are ineffective for staining purposes.

The cells are Stained by Silver salts. & Silver impregnation techniques are widely used hence the name (Argyrophilic).

The cells are also characterised by their ability to take up Bichromate Salts & impart a distinctive color. (Enterochromaffin cells). The cell types involved are:

C cells in Thyroid.
Melanocytes inskin
Respiratory epithelium; Kultchitsly cells; Lungs
Gastroentero pancreatic system; GIT A, D, B, G, Non beta cells,
Gastric glands, Pyloric glands & Islets of Langerhans

The cells have the ability to store & release a wide variety of neuroendocrine substances withdiverse functions. The Proven & the Candidate substances.

Proven	**Candidate**
Serotinin	Pancreatic Polypeptide
Histamine	Motilin
Dopamine	Chromagranin
Bradykinin	Dense Core granules
Tachykinin	ANP
VIP	Synaptophhsin
	Neuron Specific Enolase
	Entero glucagon

The clinical importance of these diffuse cell populations stems fromt the fact that when these cells undergo unopposed proliferation they result in production of a number of neoplastic syndromes & Tumors which a clinican should always bear in mind while evalvating a patient with both typical as well as atpyical signs & symptoms.

Tumors of APUD SYSTEM:

GIT: Carcinoid Tumors,
Zolinger ellison Syndrome
VIPoma
WDHA Syndrome

- Thyroid: Medullary Crcinoma Thyroid
- Skin: Multiple Myloma
- Adrenal Medulla: Phaeochromocytoma (10% Malignant,

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10% in children, 10% bilateral, 10% familial, 10% calcify, 10% extra adrenal)

- Multiple Endocrine Neoplasia 1 (Wermers Syndrome)
- Multiple Endocrine Neoplasialla (Sipples Syndrome)
- Multiple Endocrine NEoplasia IIb
- CNS: Chemodectoma,
  Paraganglionoma
  Neuroblastoma

These neoplasms can present with different signs & symptoms ranging from mild diahorrea to serious symptomology such as cardiac & cerebral damage due to malignant hypertension, cardiomyopathy, CHF & metastatic disease. Hence a need for bearing these unfortunate diverse groups of proliferations in mind which are scaterred in our bodies as stars in sky.

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TUBERCULAR BRAIN ABCESS

M.L. Babu M.Ch.; Shavinder

It is estimated that 8.8 million cases of tuberculosis occur worldwide per year, 95% of them in developing countries. Factors like HIV infection, immigration, low socio-economic status are responsible for such high incidence. Virtually all organs in body are affected. CNS tuberculosis presents mainly as tuberculoma or Meningitis. Tubercular brain abscesses are highly uncommon. Now and then case reports of tubercular brain abscess have been reported.

We report two adults, one male and other female aged 40 years and 35 years respectively who were admitted with high degree of fever, headache and vomiting. There was past history of pulmonary tuberculosis in one. Examination of patients revealed toxic looking patients, febrile with signs and symptoms of raised I.C.T. CT showed a hypodense lesion with enhancing ring. Patients were diagnosed pyogenic abscess and in both cases abscess was drained in emergency. Anti-biotics did not improve general condition. A repeat tap of pus was done and pus was sent for AFB staining. AFB came +ve. Patients were put on antibubercular treatment. Within a week fever settled and patients were discharged after ten days. In follow up both patients are doing well.

Thirty years male working in B.S.F. was admitted as a case of Gait disturbance, patient had on examination cerebellar signs. X-ray chest showed old healed tuberculosis of Lung. C.T. showed a hypodense lession in Rt. carebellum with minimal ring enhancement. A dignosis of low grade Astrocytoma was made, patient was subjected to Posterior fossa craniotomy. Pus was aspirated by ventricular cannula at suspicious area. Abscess was subsequently excised. Examination of pus confirmed A.F.B. and histology of abscess well confirmed tubercular pathology. Patient was put on antitubercular treatment, patient was discharged from hospital after two weeks. In follow up patient is doing well.

In places where tuberculosis is endemic like India, intracranial tuberculoma comprise as many as 10% of all ICSOL. In children this figure may touch >20%. Intracranial tuberculosis accounts for 0.2% cases in Western World unlike developing countries. Tubercular meningitis is an important manifestation with high rate of mortality and morbidity. Diagnosis mainly based on clincial features; CSF changes and imaging characteristics. Bacteriological confirmation is not generally possible. Tubercular brain-abscesses are very rare. Only 57 cases of tubercular brain abscess were found in a review of world literature by Whitener et al[1].

Revens-croft et al[2] reported tuberculous granutoma in childhood tubercular meningitis. A fatal tubercular abscess in an immuno-competent patient was reported by megarbane et al[3] from France.

Intraventricular haemorrhage due to rupture of PICA aneurysm in tuberculosis meningitis was reported by Griffitis et al[4]. Paradoxical appearance of tuberculoma and formation of cerebellar abscess in a patient with human immuno-deficiency virus treated with Triple anti retroviral therapy was reported by Seijo-Martinez et al[5].

Arestis N et al[6] had population based study of children with cerebral tuberculosis. They observed TBM and tuberculoma in their study but not a single case of abscess.

Gazzaz et al[7] reported a tubercular cerebellar abscess and Barber et al[8] presented a case of raised ICT secondary to non-thrombotic obstruction of the superior sagittal sinus by a midiline tubercular abscess. Mohanty et al[9] presented "S.T. aspiration" as a useful alternative modality in management of tubercular abscesses in selected cases. A single case of carebellar abscess was reported by Oshinowo and Schoenan[11] Tang et al[12] reported a case of multiple tubercular abscesses in a child who had tuberculous meningitis.

Upadhayey et al[13] reported multiple tubercular abscesses following V.P. shunt for post T.B.M. hydrocephalus.

Tubercular abscess as a complication in HIV infected case was reported by Gettler et al[14]. They reported evolution of tubercular abscess on prolonged ATT therapy. An Intracranial tubercular abscess mimicking Glioma was reported by lidan[15] et al. Shintani[17] et al reported a tubercular brain infection in an old cerebral infarct. Three cases of tubercular abscess were reported by Parkash[18] et al in brain stem. Reichenthal[19] et al reported C T morphology in tubercular brain abscess.

Though tuberculosis in CNS occurs due to haematogenous spread of M. tuberculi from else where; TBM can also occur via Lymphatic spread from Cervical nodes. Tubercle bacilli are immobilized in end-arteries which lead to formation of sub meningeal tubercular foci. Meningeal surface gets covered by yellowish grey exudate.

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In tuberculoma bacilli get lodged in brain with rich blood supply. Once tuberculoma is formed, it evokes secondary reaction which leads to formation of thick capsule. Surrounding brain oedema and low gliosis may resemble low grade Astrocytoma. In rare cases there may be Central Caseation, liquefaction and formation of an abscess. This phenomenon is very rare. tubercular brain abscess occurs commonly in patients with abnormal cell mediated immunity and are mostly focal. These lesions are secondary to Lung disease and at junction of grey and white matter. Tubercular abscess is devoid of granulomatous reaction associated with tuberculosis. Histologically and clinically these abscesses are similar to pyogenic abscesses. The abscess wall is composed of necrotic inner surface and a fibrous outer surface associated with an inflammatory reaction. Criteria for diagnosis are:

- Pus within brain
- Bacteriological Proof or
- Histologic confirmation of abscess.

Their presentation is acute; often in 3rd or 4th decade. These are mainly supratentorial and rarely in cerebelium. These present with focal neurological signs and are associated with histoligical and Laboratory evidence of tuberculosis. Laboratory data shows, high ESR; CSF has pleocytois with increased protein; PCR +ve in good number of cases. Tubercular abscess should be differentiated from Cystic tuberculoma. In this unlike pus cyst contains yellowish fluid and cyst wall has typical tuberculous pathology.

CT shows hypodense lesion surrounded by enhancing ring. There may be associated surrounding oedema. At times it becomes difficult to differentiate tubercular abscess from pyogenic abscess on the basis of clinical; roentgenologic findings. AFB shpuld be demonstrated on Ziel Nielson stain. Appropriate treatment includes anti-tubercular treatment with surgical excision / aspiration.

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FINE NEEDLE ASPIRATION; DIAGNOSIS OF NODAL HODGKIN'S LYMPHOMA (PART II)

A.R. Khan; Shuab Omer; Sumia Rashid; Syed Besina

Abstract: *6620 lymph nodes were aspirated over 11 yr. period (Jan. 1991 - Dec. 2001) yielding 345 lymphomas. This included 90 cases of HL (26%). Out of these only 76 cases (84.4%) were diagnosed by FNA irrespective of sub typing. A suspicion of disease arose in 6 cases (6.7%). Smears were negative with picture of reactive lymphadenitis in another 8 cases (8.9%). This was attributed to scanty material in the aspirates. Subtyping attempted showed a correlation with histology in 50 cases (>55%). The cytohistopathologic correlation was best seen in lymphocyte predominant and mixed cellularity subtypes. Diagnosis and subtyping of NSHL was more difficult. There was only one case of lymphocyte depletion reticular disease correctly diagnosed on FNA. Most of the cases were recorded in first and third decade with male predominance at all ages.*

Key words: *Fine Needle Aspiration (FNA) Hodgkin, lymphoma (HL)*

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Introduction

Gutherie[1] was the first person to diagnose Hodgkin's lymphoma in 1921. This was followed by a few reports before more precise classification of the disease appeared in the literature.[2-5] However these classification have been revised more recntly.[6-7] The publications on the subject after 1966 are more relevant.[10-13] Sensitivity and specificity of FNA in Hodgkin's lymphoma are lower than non-Hodgkin's lymphoma.[10-11] FNA is only of limited value in primary diagnosis and subtyping of Hodgkin's lymphoma but can be diagnostic in recurrent disease.[11] Surgical biopsy is considered necessary for the primary diagnosis of the disease.[12]

Authors review here the FNA material of 11 years (Jan 1991- Dec. 2001) on the subject based on 6620 lymphnode aspirates.

Materials and Methods

FNA was done in 6220 lyhmphnodes over 11 years period (Jan 1991 - Dec. 2001) using 10-20 ml disposable syringes with and without syringe holder and 22-24G disposable needles. Material aspirated with 3-4 passes was spread over 3-6 slides. Air dried smears with MGG stain were used in all cases, wet alcohol fixed H&E in some and PAS stains in selected cases only.

The aim of FNA was the diagnosis of lymphoma, non-Hodgkin's and Hodgkin's and their delineation from infectious/tuberculous and metatastatic disease. The subtyping of Hodgkin's lymphoma was not the primary aim. However a record of the attempted subtyping was maintained in the personal files.

Smear diagnosis of the Hodgkin's lymphoma was based on the tumor cells and the reactive cellular component. The tumor cells comprised of classic bi-or multinucleated cells, mono-nuclear Hodgkin's cells, popcorn cells, large polypoid cells and pleomorphic giant cells. The reactive cellular component comprised of lymphocytes, histiocytes, plasma cells, eosinophils, neutrophils and fibroblasts. The type of the tumor cells and cellular company varied according to the subtype paralleling the tissue description.[15]

The lymphocyte predominance nodular Hodgkin's lymphoma (LPNHL) diagnosis in smear was based on the presence of popcorn neoplastic cell with and without histiocytes and numerous lymphocytes in the back ground. The diagnosis of classic mixed cellularity Hodgkin's lymphoma was made on classic R-S cells with or without other variant tumour cells and a mixed infiltrate of lymphocytes, histiocytes, plasma cells, eosinophils, neutrophils and fibroblasts. The diagnosis of NSHL (nodular sclerosing Hodgkin's lymphoma) was based on large multilobulated R-S cells with varying number of R-S variant cells and reactive inflammatory cells. Diagnosis of lymphocytic depleted reticular type (LDHL) was made on pleomorphic R-S cells, with variable number of reactive cells. (Fig. 1-8).

Results:

Disease pattern based on 6620 lymph node aspirate is

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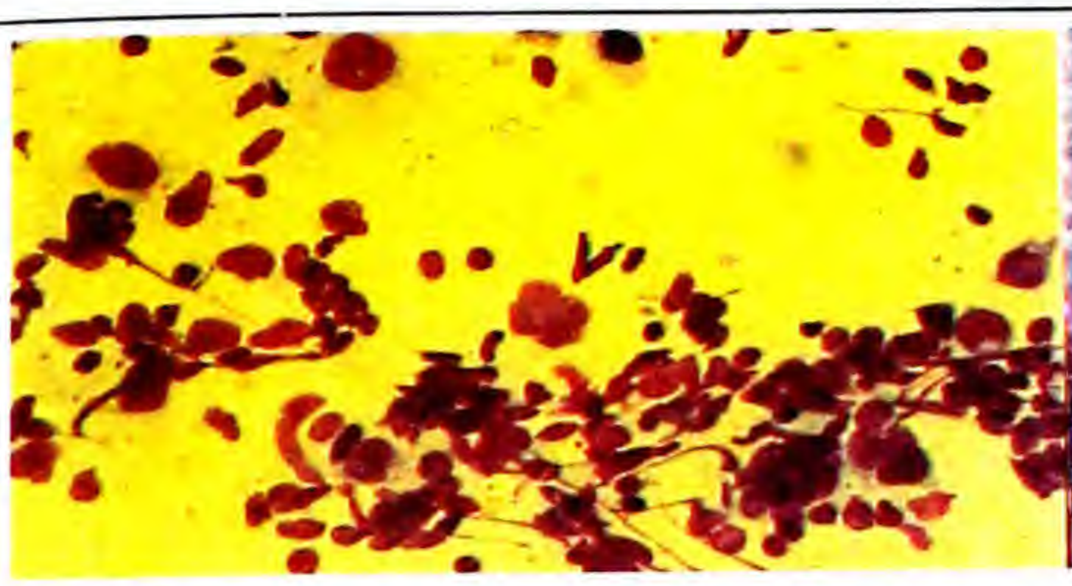

Fig. I: H.L. Lymphocyte predominance, shows R-S variant popcorn giant cell (arrow) and small lymphocytes. MGG x400

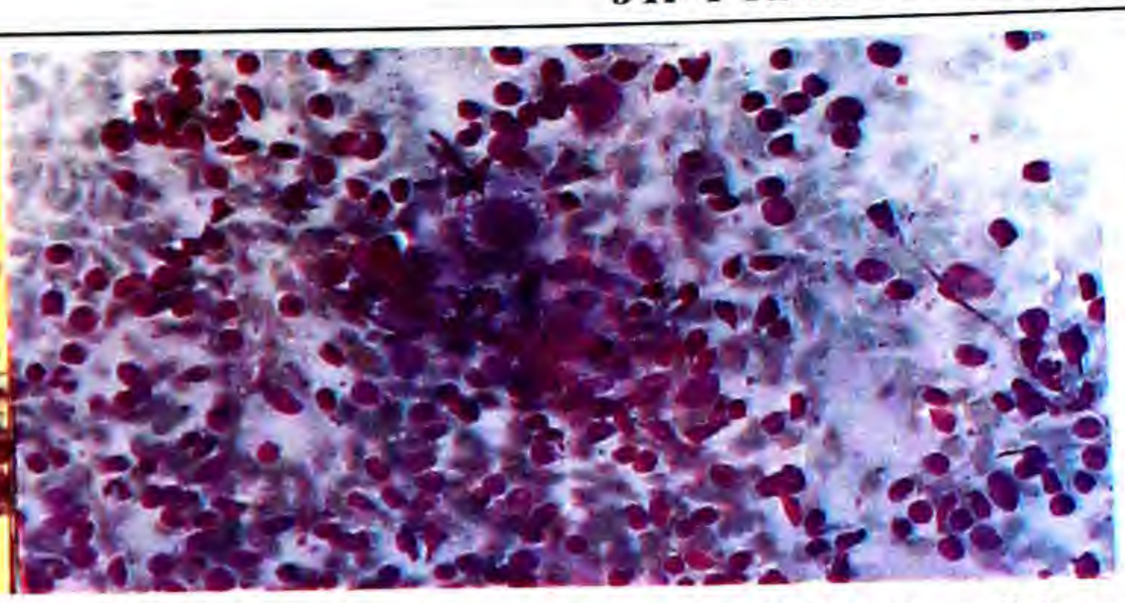

Fig. 2: H.L. shows a mononuclear Hodgkin's cell (arrow) with reactive cells. MGG x400.

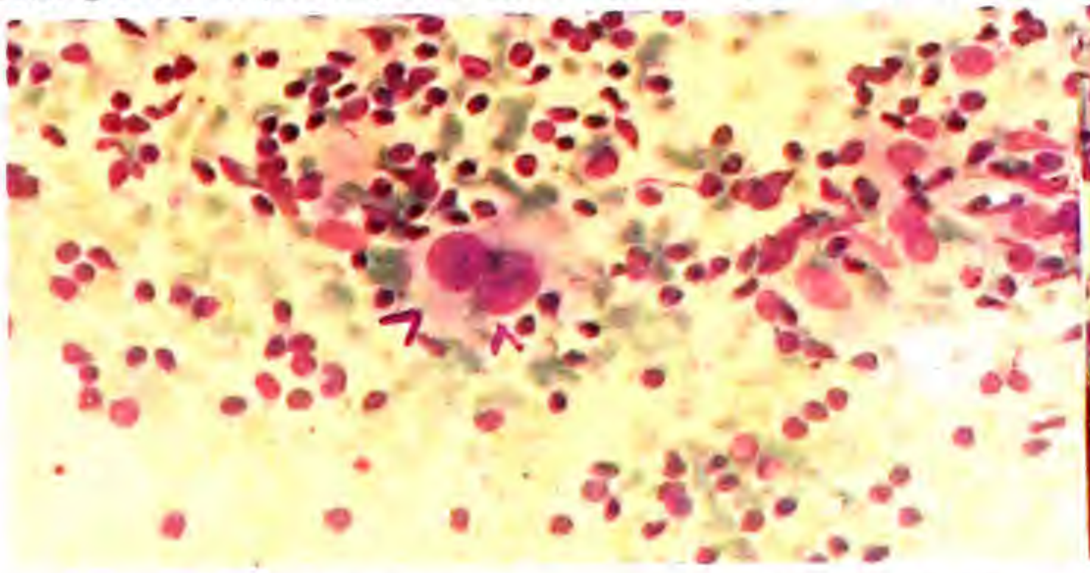

Fig. 3: H.L. mixed cellularity, shows a classic binucleate giant cell (arrow), lymphocytes and eosinophils. MGGx400

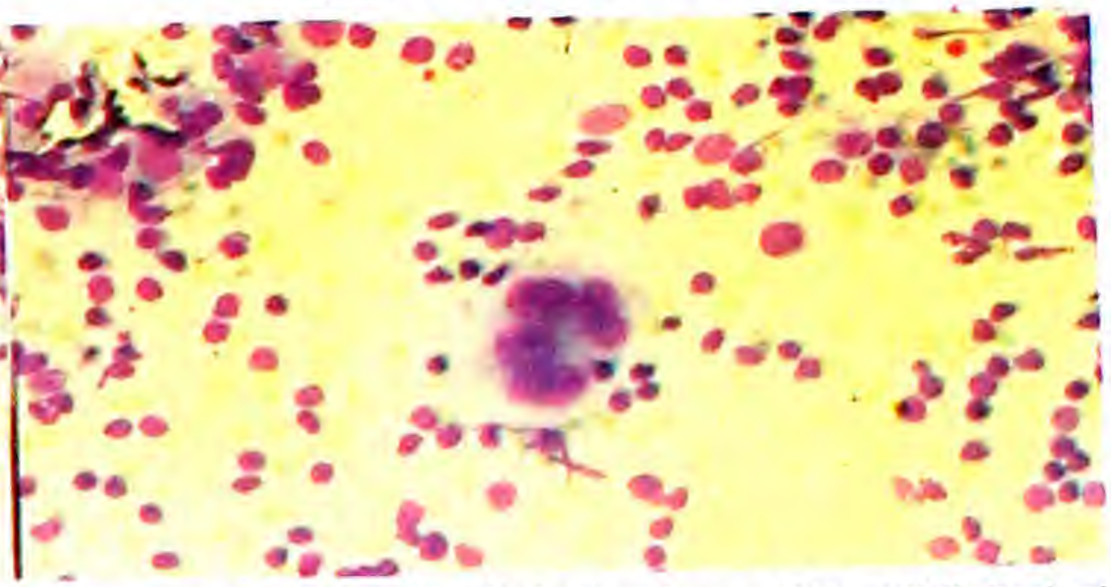

Fig. 4: H.L. Mixed cellularity-shows R-S multilobed giant cell and many lymphocytes. MGG x400

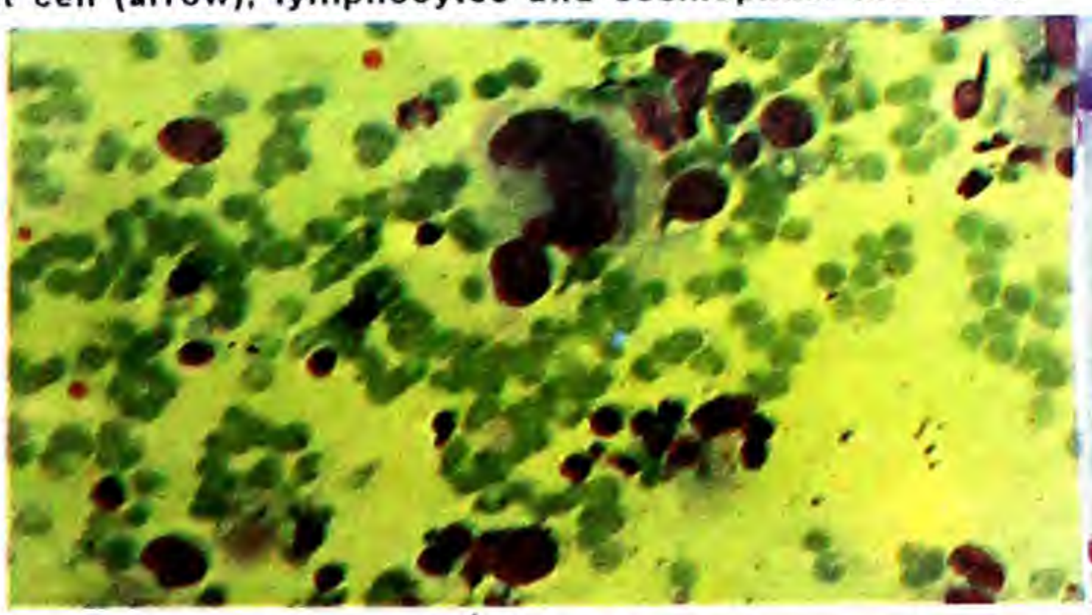

Fig. 5: H.L. Mixed cellularity-shows R-S cell, with multilobed nucleus, mononuclear cells and lymphocytes. MGGx400

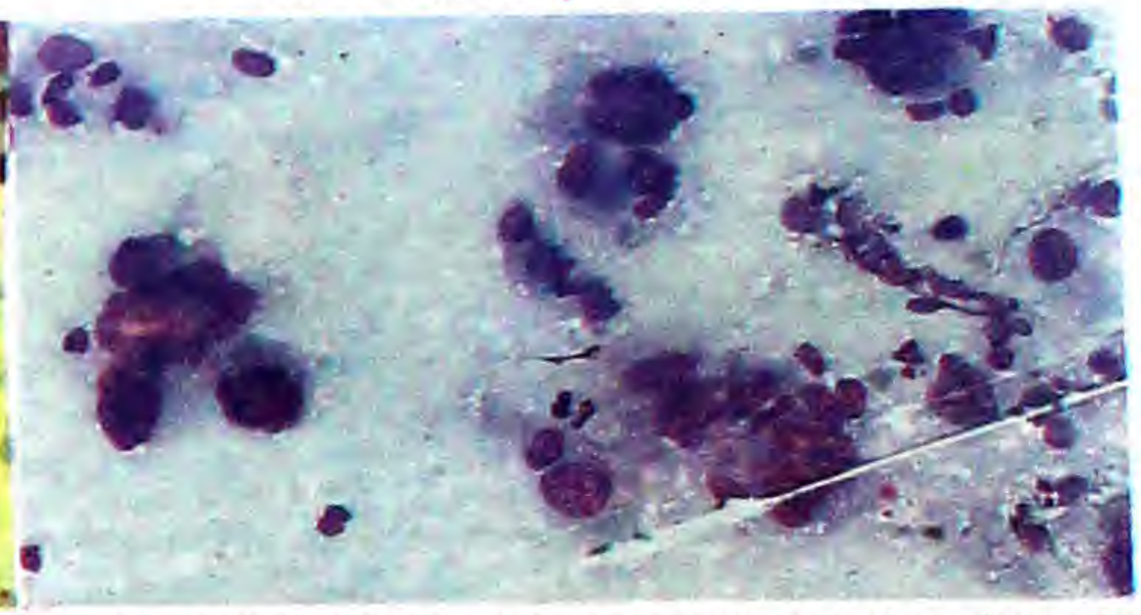

Fig. 6: H.L. Lymphocyte depletion, reticular, shows large pleomorphic giant cells, mononuclear Hodgkin's cells and a few lymphocytes MGGx400

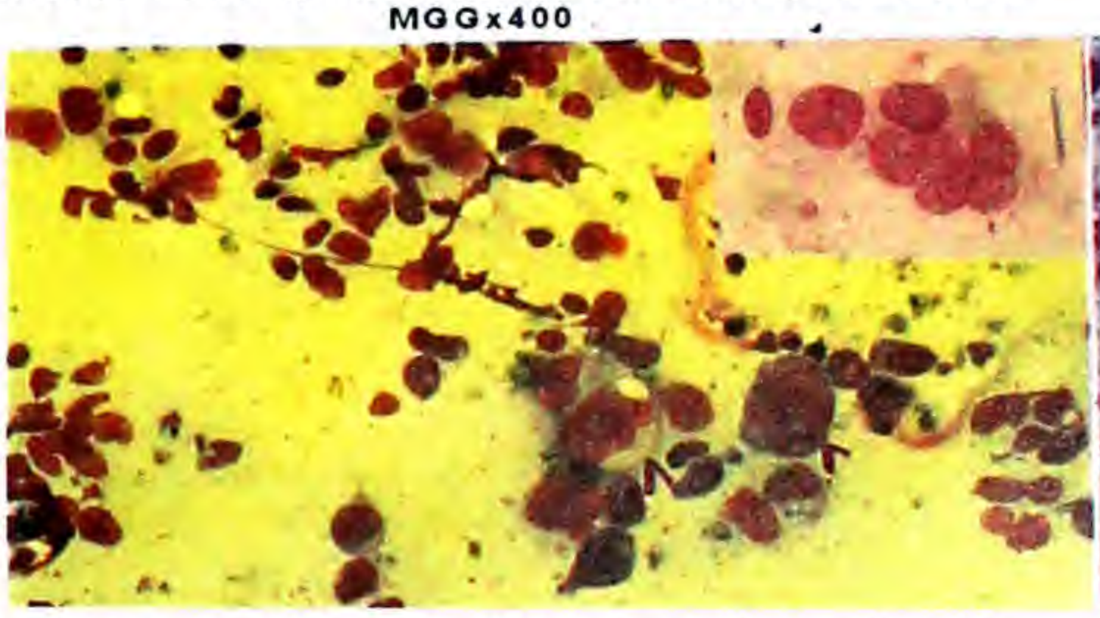

Fig. 7: H.L. nodular sclerosing, shows giant cells with polypoid nuclei, few binuclear cells, lymphocytes and cosinophils. Inset shows a polypoid lacunar giant cell-MGGx400

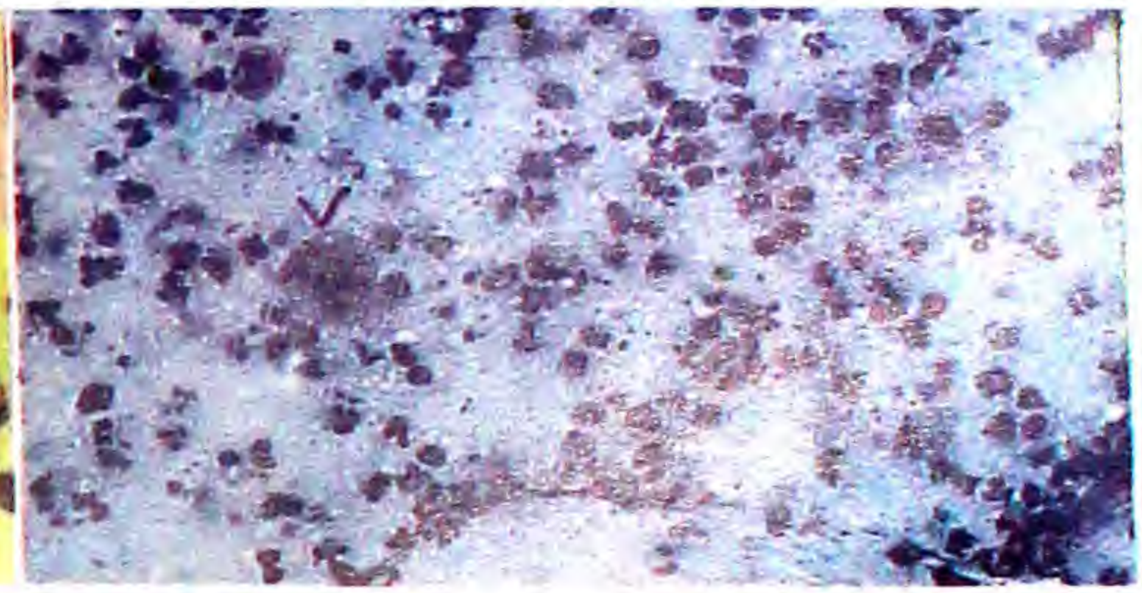

Fig. 8: H.L. mixed cellularity, with tuberculous lymphadenitis, shows a binuclear classic giant cell (arrow) with many neutrophils and necrotic debris (it was also AFB positive) MGGx400

given in table 1. Out of 345 cases of primary nodal lymphomas, there were 90 cases of Hodgkin's lymphoma (Table-2). The age, sex and anatomical distribution of these 90 cases are given in table3. 28 cases (31.1%) were seen in children aged 1-14 yrs and out of theses 21 cases (>23%) were seein the first decade. Sixty two cases 68.9% were seen in persons above 14 yrs, with 19 cases (21%) constituting second peak in third decade. In children, male to female ratio was 4.6:1 where as in age group above 14, it was 2.26:1. Cervical lymphnodes (80 cases) were the most common sites of aspirate. All the 90 cases were subjected to excision biopsy of the representatives nodes. Quality of smear pattern is given in table 4. Thus in 76 cases (84.6%) smears were diagnostic of Hodgkin's lymphoma. In 6 cases, smears were suspicious. In another 8 cases smears were negative, with scanty cellular material composed of reactive lymphoid cells only. These normally could be excluded from the analysis by some authors. However, we have not done so. In this group on histopathology there were 4 cases of mixed cellularity, one of these was a 3 yr old non-cooperative child with small posterior cervical nodes. Another 4 cases proved that of NSHL. One of these reaspirated after 3 months was diagnosed as HL with no clue to sub typing.

In 4 cases there was association with tuberculosis. In 2 cases it was interesting to see both Hodgkin's lymphoma and tuberculosis in the same aspirate in left axillary node in one case and in left supraclavicular node in another case. (Fig. 8).

Discussion:

Hodgkin's lymphoma has undergone many classifications since its first description by Thomas Hodgkin[16]. The malignant nature of the disease though recognized for long time has received a firm support only recently by demonstration of clonal nature of the R-S cells[17,18,19]. Immunophenotype and more recently molecular genetic studies have shown that nodular and mixed cellularity subtype express B-cell associated antigens as well as rearranged immunoglobulin genes thus confirming that not only lymphocyte predominant nodular Hodgkin's lymphoma (LPNHL) but also most cases of the classic Hodgkin's lymphoma represent neoplastic B cell disorders[18,19]. It is also believed now that most instances of lymphocyte depleted Hodgkin's lymphoma represent large cell anaplastic CD 30 positive non Hodgkin's lymphoma[8,21]. This entity now represents less than 1% Hodgkin's lymphoma[8].

Hodgkin's lymphoma on lymphnode puncture was first diagnosed by Gutherie[1] in 1921. Many reports of FNA in Hodgkin's lymphoma have since appeared in the literature[2-5,10-13]. In a total of 90 cases of nodal HL aspirated, correct diagnosis was possible in 76 cases (84.4%). Smears were suspicious in 6 cases (6.7%) and negative in 8 cases (8.9%). In suspicious smears, tumour cells were atypical but typical R-S cells were not seen. In the 8 cases of false negative the cellular yield was scanty and insufficient to make any diagnosis obviously due to fibrosis of the nodes.

Table-1: FNA Lymphnode Results

Cytological DX.	Patients No.	Percentage
1. Reactive/Infectious (nontuberculous)	3628	54.80
Tuberculous	1994	30.12
Metastatic Malignancy	490	7.40
Lymphoma (primary nodal)	345	5.21
Inconclusive	163	2.46
Total	**6620**	**100%**

P.S. Extra nodal lymphomas and those reaspirated for residual and relapses are excluded.
DX - Diagnosis

Table-2: FNA 345 cases of Nodal lymphomas

Type	No. of cases	%age
1. Non-Hodgkins Lymphoma	255	74%
2. Hodgkins lymphoma	90	26%
Total	**345**	**1005**

Table-3: FNA of Nodal Hodgkin's lymphoma

Age (Years)	M	F	CX.	AX.	ING.	ABD
1-9 years	17	4	20	1	0	0
10-14 years	6	1	6	0	1	0
15-19 years	7	2	7	0	2	0
20-29 years	13	7	18	12	0	1
30-39 years	11	3	13	1	0	0
40-49 years	8	3	8	1	1	0
50-59 years	4	3	6	1	0	0
60-69 years	0	1	1	0	0	0
70-79 years	1	0	1	0	0	0
Total	66	24	80	5	4	1

Abbreviation:
CX - Cervical
AX - Axillary
Ing - Inguinal
ABD - Abdominal

Table-4: FNA in Nodal Hodgkin's lymphoma

	No. of cases	Percentage
Diagnostic	76	84.4%
Suggestive / suspicious	06	6.7%
False Negative	08	8.9%
False Positive	0	
Total	90	100%

The smear diagnosis of the Hodgkin's lymphoma depends on the adequacy of the material, quality of stained

smears, experience of the interpreter, subtype of Hodgkin's lymphoma, size of the node and the anatomical site. Thus in superificial easily accessible nodes like cervical, axillary or femoral, there was invariably no problem in getting representative material in lymphocyte predominant and mixed celluarity subtype. The nodular sclerosing classic did not yield adequate representative material. In syncytial variant of nodular sclerosing Hodgkin's lymphoma, smears mimic[8] metastatic carcinoma. The lymphocyte depletion being a rare disease[8] yet an odd case with pleomorphic tumour cell rich may not give any clue unless typical R-S cells are found. We had one such case in the study (Fig 6). In cases with atypical tumour cells and mixed reactive cellular infiltrate, differentiations may be difficult from metastatic anaplasatic carcinoma, particularly in cervical nodes with primary from nasopharynx. In such cases, immunocytochemistry on smears or immunohistochemistry on cell blocks may be helpful. Alternatively, the excision of the representative node becomes mandatory.

The sub typing was possible in most cases (50 cases) of lymphocyte predominant and mixed cellularity subtypes. The nodular sclerosis was most difficult to subtype. We agree with the findings of Dass et al[11] that FNA has a limited role in subtyping of Hodgkin's lymphoma. We believe that primary diagnosis of Hodgkin's lymphoma is crucial rather than sub-typing, since all diagnostic/suspicious smears are subjected to excision of the representative nodes.

Though the study many not reflect the exact disease pattern here in Kashmir, this study shows that lymphocyte predominance and mixed cellularity are most common subtypes and nodular sclerosis subtype comparatively rare disease, a total contrast with the west.

Age and sex pattern are also different from western Hodgkin's lymphoma. Most of our cases occurred in first and third decade with male predominance at all ages (table 3).

In summary, FNA diagnosis of primary nodal Hodgkin's lymphoma is a useful, quick, cheap, and reliable diagnostic procedure in smear positive cases in experienced hands which allows quick planning and treatment. Subtyping is neither highly predictive nor essential since all representatives nodes dictated by FNA are excised for histopathology. Persistent significant nodes need follow up/ excision to avoid delay in diagnosis and treatment.

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HEPATITIS B; GLOBAL EPIDEMIOLOGY, CONTROL STRATEGY AND VACCINATION:

It was interesting to read the article on the above mentioned subject in the recent issue of JK-Practitioner[1]. Author has carefully outlined the global prevalence and different control strategies and has also tried to explain the Hepatitis B situation in our homeland (Kashmir). Hepatitis B is creating havoc in sub-Saharan Africa and South East Asia. Even in Middle East, where the prevalence of hepatitis B is 7-10%, the people have developed, what has been commonly called Hepatic hydro-chondriasis, due to large number of patients coming with acute hepatitis, chronic hepatitis, hepatitis B carrier, recurrent G.I. bleeds, ascites and enchaphalopathies. When patients develop hepatomas, it is a miserable situation to watch. Even the medical care personal have become hyper-sensitive to the possibility of developing hepatitis B infection form their patients, by needle pricks or mucosal splashing of blood. They take all possible precautions, to save themselves. There are infection control committees in each and every, big or small hospital, usually with one infection control officer and many infection control nurses. All needle pricks and accidental splashing of skin or mucus membranes are immediately reported and action started as soon as possible according to established guidelines. Although we do not have exact prevalence rates of hepatitis B in our community (Kashmir) available, but as the author has mentioned it is not a reason for an alarm here. But then there is a point in the process. Those conditions which are a reason for concern to our medical community here (esophageal malignancy; gastric malignancy or diarrheal diseases & tuberculosis), we do not have any reliable preventive method available like we have heptitis B vaccine for hepatitis B. In case of gut malignancies, even the physicians and gastroenterologists are all confused and frustrated as to what can be done to prevent these types of problems. They all become helpless infront of their patients seeking reasons for etiology or prevention. Hepatitis B, though not of community significance but is at least a preventable disease. As the dictum goes in clinical medicine "look for treatable causes first" so could be at community level — "plan for the preventable disease first." As far as safe methods of clinical practice in hospitals and clinics goes, I think there should be no second opinion. We should start establishing infection control committees in all the hospitals, keep separate containers for sharps that must be available in all major wards and clinics, follow strict universal precauions, have color coded disposable containers for all types of medical waste and tissue according to established guidelines. However the precess does not end up there. We have innumerable clinics, laboratories and small nursing homes virtually under no bodies' control. Those set ups have also to be brought under this scheme through health department.

One of the points, which needs to be emphasized in hepatitis B vaccination is education and training of physicians and paramedical staff involved in the implementation of program. Most of the people involved in the process seem to know very little about the disease or the vaccine and its proper use. Knowledge about the program is more important for its successful implementation, because "what mind does not know eyes can not see." More depressing & shocking would be the news that at many centers patients were given tetanus toxoid instead of hepatitis B vaccine and in some centers hepatitis B vaccine was reportedly sold to private parties. There have been reports in local press about the mismanagement of vaccine distribution at various health centers. Department of Health Services has to do a lot of groundwork in order to achieve the desired results. Otherwise it will be another futile exercise.

Angels will not come from skies to rectify our problems and solve our sufferings. Let us all work together to put all malpractice aside and provide quality services to our people. Here I would like to remind all my seniors and colleagues about the need for a "Professionals Forum" to be crowned by senior professors as suggested earlier.[2]

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JK-Practitioner 2002; 9(4): 268

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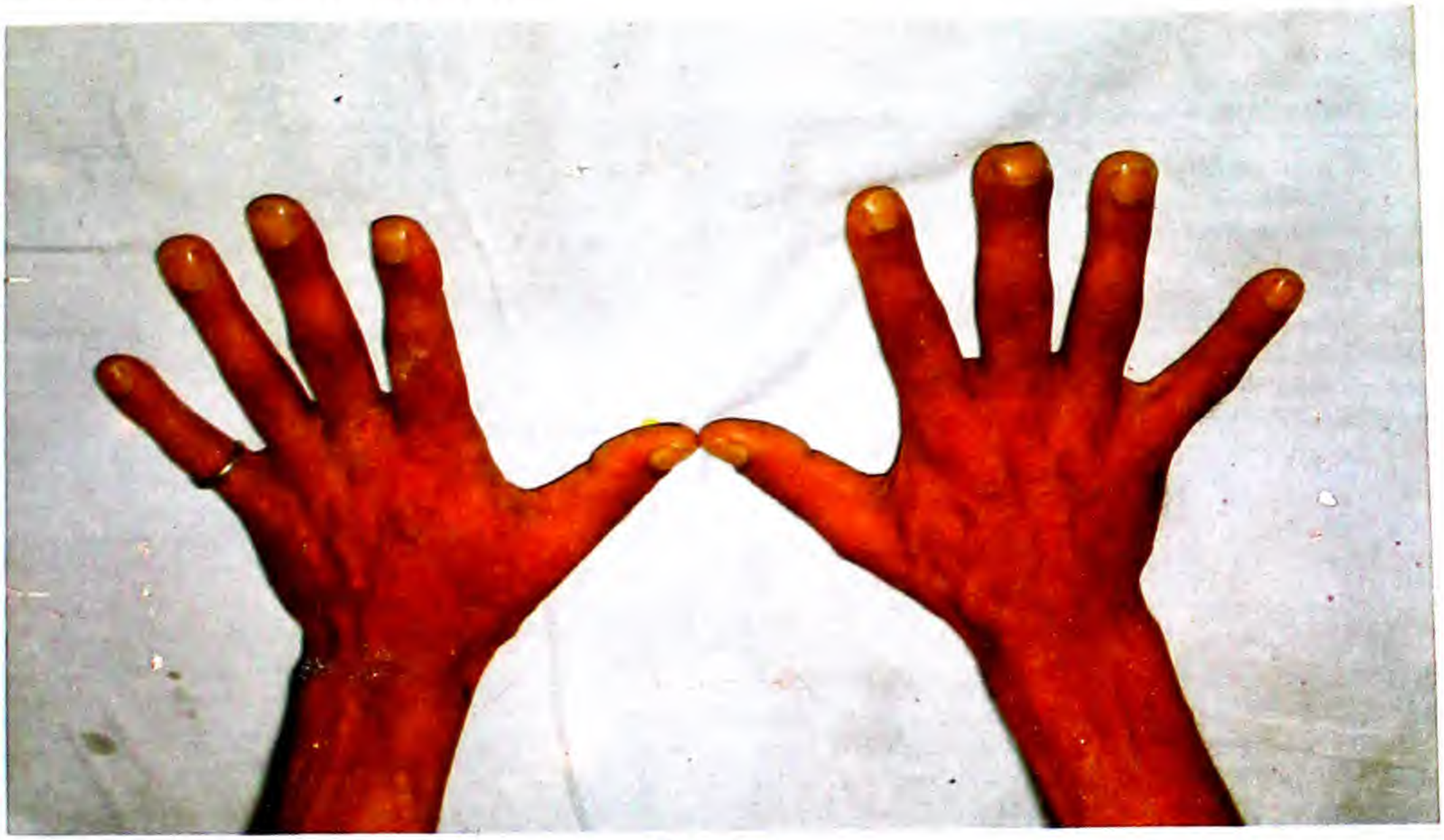
CLINCH THE DIAGNOSIS



Questions

A 42 year male was admitted with diagnosis of Acute Viral hepatitis with subacute Hepatre failure.

A. ***What principal abnormality is seen in the fingers?***

B. ***What is the likely cause?***

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Answers on Page 284

THE SESSAMOID BONES

Abdul Ahad M.D., Masarat Rasool MBBS, Shameem Jabeen MD

The word sessamoid is derived from the Greek word" SESAME" meaning seed like. this seed may just be firroconnective tissue or as a cartilage or get ossified to form the bone.

The sessamoid bone differs from the other bones in 1. These have no periosteum 2. have no medullary cavity 3. Have no Haversian system. 4. These are mostly found in relation with the joints and their articular capsules in particular. Some authors consider that these sessamod bones are primarily articular in nature i.e. these are embedded in joint capsules and their association with the tendons is secondary.

Phylogenitically in reptiles these form the integral part of the skeleton. Phylogenic and local causes are held to be responsible for their development. It has been seen that patella develop at the site of implantation of limb bud of chick embryo in chorioallantoic membrane. It has also been seen that removal of dogs patella leads to the development of an another patella at the site of removal. These bones may join together to form traction epiphysis e.g. in the upper part of olecranon. The sessamoid bones are not always completely ossified. Ossification begins late in the life as compared with other bones i.e. during 12-18 years in males and 3 years earlier in females. There are exceptions e.g. patella ossifies from several centres during 3-6 years of age. This determination is difficult as the races differ and are mixed. The data available has been collected in caucasians.

The sessamoid bones have important functions. 1. These mordify the pressure exerted at the sites of their presence. 2. These modify/reduce friction. 3. These alter the direction of pull of a muscle e.g. patella streamlines the pull of the four heads of quadriceps femoris just like flexor accessorius which has the similar effect on the flexor digitorium longus. 4. The sessamoid bones help to maintain local circulation by providing resistance to the pressure or weight thus releasing the same pressure that could collapse or partially block the adjoining blood vessels e.g. in foot during standing or running. We have classified the sessamoid bones into three groups.

A. Sessamoid bones in relation with the joints
   I. In upper limb
   II. In lower limb
B. Sessamoid bones which are not in immediate relation with the joints.
   I. In upper limb
   II. In lower limb
C. Articular Sessamoids.

Curiously enough the sessamoid bones are not found in relation with the joints of the central (Axial) skeleton.

A. I. Upper Limb:-

1. In the tandons of flexor pollcis brevis and adductor pollicis.
2. Interphalangeal joints of the thumb (73%).
3. Metacarpophangeal joint of the 5th digit (Minimus) (70%)
4. Metacarpophalyngeal joint of the index (35%)
5. Metacarpophralyngeal joints of the 3rd and the 4th digit (Medius and annulus).

A. II. Lower Limb:-

1. Patella
2. Tendon fo flexor hellucis brevis in both the heads (These may be duplicated to look as four sessamoid bones in the two heads of the muscle.
3. Metatarsophalangeal joints of all the toes.
4. In the interphalyngeal joint of the great toe.

B. I. Upper Limb:-

1. Occasionally in the tendon of biceps brachii near its insertion.

B. II. Lower Limb:-

1. Iliacus where it passes over ilium.
2. Gluteus maximus where it passes over the greater trochanter.
3. Tendon of peroneus longus under the cuboid bone.
4. Tibialis anterior near the anteroinferior part of the medial cuneiform bone medially.
5. Tibialis posterior near the head of talus.
6. and 7. in tendons related to medial and the lateral malleoli.

C. Artricular Sessamoid:-

1. In the tendon of the lateral head of gastrocnemius (Fabella). When present it articulates with the lateral Condyle of femur.

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STICK TO YOUR SYSTEM OR SUFFER "CROSS BORDER" PRACTICE AXED BY SUPREME COURT

Nisar Ahmad Bhat M.D.

Introduction:

There has been a global revolution in the drug development in the last five decades since world war II[1]. This has been made possible by the whole hearted efforts of the pharmaceutical industries (PI) through out the world. More than 5000 drugs and 45000 formulations are there in the Indian market[2]. Pharmaceuticals (PI) through out the world are heavily involved in aggressive drug promotions, with a clear aim to change the prescribing habits of physicians and to encourage self medication of patients. One of their important targets for promotion is the doctor where repeated attempts are made to generate more prescriptions by changing the prescribing behaviour of physicians[3]. The doctor is the decision marker for the ultimate user, the patient. This aspect of doctor patient relationship has been specifically exploited by the PI to target their effective promotional strategies. In India nearly 40,000 MR's employed by the PI might be doing this job[4]. MR,s have been well described as "Stealth bombers" of medicine, that they swoop in, change the prescribing habits of physicians and disappear again[5]. The primary goal of the MR is to promote the product but irrational approach by the doctor can put him into trouble, by using cross border medicines. There is wide spread "cross border" prescription by some allopaths who encroach into Ayurvedic formulary. Similarly some vaids, Hakims and Homeopaths do not hesitate to use modern drugs to get quick results. Allopaths are not acquainted with the knowledge and skill required to produce such 'customized' formulations for individual patients. The entry of commercial enterprises producing branded Ayurvedic formulations has changed the scene. Taking full advantage of the laxity in enforcement laws, medical representatives regularly call on allopaths to seek patronage for Ayurvedic medicines. To impress Allopaths some producers have gone even to the extent of getting their Ayurvedic brands subjected to "Clinical Trials" in allpathic medical colleges. Because of their prescription power, the principal targets for promotion are allopaths. Therefore many manufacturers of ayurvedic medicines label their brands exclusively in English with indications borrowed from books of modern medicine. Other wise why do they not use the traditional names of diseases such as Prameha (diabetes), Mutraglata (urinary flow reduction), Mutra-Kracchra (painful micturation), Yekrit roga (liver disease) etc in Devangari with which Ayurvedic practitioners are more familiar.

Apex Court Judgment and case summary[6]

The case in point involves a registered Homeopath medical practitioner of Bombay. While treating a patient he prescribed some allpathic drugs. When the condition of the patient showed no improvement he was shifted to a large hospital where subsequently he died. The patients wife approached the National Commission under the Consumer Protection Act for compensation against the said doctor on the ground that he was negligent in treating her husband. The National Commission did not find merit in the case and rejected her application for compensation.

The matter went in appeal before the Supreme Court against the decision of the National Commission.

After analyzing provisions of various Acts the Supreme Court held that the doctor in question was allowed to practice homoeopathic system of medicine only but he exceeded the area of his practice and there by committed negligence and hence was liable to be prosecuted. Firstly he did not hold any qualification in allopathic system of medicine and secondly, he was not entitled under the relevant law to practice as an Alopath. The court observed that a person having studied one system of medicine can not possibly claim deep knowledge about drugs of other systems. The doctor was therefore proclaimed as a quack and a mere pretender to medical knowledge or skill and imposter (charlatan). The doctor was held to be negligent and ordered to pay rs. 300,000 as compensation and Rs. 30,000 as legal costs to the wife of deceased. In addition, the Medical Council of India was directed to initiate proceedings against the 'quack' for having illegally practiced in allpathic system of medicine. He also faces action for professional misconduct under rules applicable to registered homoeopaths.

Implications for Doctors and pharmaceutical Industries

The impact of the said judgment by the nation's highest court would directly affect doctors who prescribe

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medicines from other systems in which they are not registered. They should desist from doing so. The Supreme Court has ruled that exclusiveness of each system of medicine has to be respected. The ruling will reduce the unhealthy and unethical practice of encroaching into other systems of medicine to meet competitive needs of the medical practice.

In the light of the Supreme Court judgment, those medical practitioners who prescribe medicines from other systems will be considered quacks and deemed to be negligent per se without any further proof or argument due to violation of statutory provisions and will consequently be liable for penalties under different laws, namely:

1. **Under civil law:**
   The medical practitioner will be liable for unlimited monetary claim from the patient or his successors if the patient has suffered any damages or has died. A suit either under Indian Contract Act 1872 or a complaint under Consumer Protection Act 1986 can filed. remedy under the latter act being simpler, quicker and economical is usually preferred.

2. **Under Medical Councils Acts:**
   Whose rules and regulations the practitioner has violated by practising without qualification and registration. Penalty includes imprisonment for one year or fine or both. The relevant provisions are incorporated in Section 15(3) of the Indian Medical Council Act 1956, Section 17(4) of the Indian Medicine Central Council Act 1970 and Section f the Homoeopathy Central Council Act 1973.

3. **Under the Practitioner's own Medical Council Act;**
   For "Professional Misconduct". His name may be removed from the register to bar him from practicing in his own system in which he is qualified and registered as per provisions section 24, section 25 and section 27 respectively of the Acts mentioned above.

4. **In case death occurs:**
   The doctor is liable to be punished with imprisonment up to two years or with fine or both under section 304-A of the Indian penal code. This section deals with "causing death by negligence."

Further under criminal law, it is not only the offender who is punished but also those who abet, instigate or conspire under chapter V of the IPC. The abettor is generally punished with the same punishment as the actual offender. If there are two or more persons involved they are all liable for punishment under chapter V-C of the IPC as conspirators.

The function of judiciary is to interpret laws as they exist. This has been done by the apex Court. It is now for the nation to find ways and means of using various systems of medicine in the best interest of the humanity. The pharmaceutical industry have the right to promote their products but it is the responsibility of the company to do so in a fair, accurate, ethical and legal manner[7]. The medical profession needs to alert and not subverted. They should maintain their own integrity and should not deviate from their own system of medicine and should not mix up different systems of medicine.

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HELICOBACTER PYLORI – THE UNIQUE ORGANISM

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Peptic ulcer disease is a common disorder of the community with an overall lifetime prevalence of around 11 percent [1,2]. It causes significant morbidity and mortality. In the United States alone, an estimated 15,000 deaths per year occur as a consequence of complicated peptic ulcer disease [3]. Over the decades we believed that peptic ulcer disease is caused by increased acid secretion as a result of increased parietal cell mass [4]. This concept gave us H2 receptor antagonists and proton pump inhibitors to block acid secretion and to treat such diseases [5,6]. It worked wonders and over the last 3 decades peptic ulcer disease became medically curable [7]. The discovery of *Helicobacter pylori (H. pylori)* by Warren and Marshall in 1983 was a landmark breakthrough in understanding of gastro-duodenal disorders [8-10]. An explosion of knowledge on *H. pylori* has changed our basic concept of all gastro-duodenal disorders and famous dictum of "no acid, no ulcer" has been replaced by "no bacterium, no ulcer" [11]. Peptic ulcer, once an acid related disease, is now classified as a bacterial disorder [12-14].

Agent

H. pylori is a curved spiral gram-negative motile organism with 4 to 6 sheathed flagellae. It is slow growing, microaerophilic bacterium, with some striking biochemical and biological features making it one of unique organism [15]. *H. pylori* is also versed with being the commonest human bacterial infection and infects around half of human population [16-18]. *H. pylori* infect gastric antrum and causes gastritis as a result of this infection (Fig 1). Body of the stomach can also be infected with or without evidence of gastritis. Involvement of gastric cardia usually leads to inflammation of this region. However the most striking feature of this organism is its inability to infect normal duodenal mucosa. In sharp contrast to this, gastric metaplasia of the duodenal mucosa is a favorite for *H. pylori* colonization. In fact it is the involvement of the duodenal mucosa, which forms the basis for *H. pylori* duodenitis, and eventually formation of duodenal ulcer [19-20]. *H. pylori* organisms cannot colonize regions of normal antrum. Intestinal metaplasia of gastric mucosa is also hostile to bacteria and *H. pylori* colonization stops sharply at the border of the metaplastic epithelium. *H. pylori* are placed in the gastric mucus and underneath it, attached to surface epithelium. Gastric pits are a favorite site for placement of the bacteria. However, *H. pylori* are not seen inside the gastric epithelial cell or in the submucosa [15]. *H. pylori* produce large amounts of urease and the enzyme a major component of the bacterium [21-23]. *H. pylori* urease is primarily a cytoplasmic enzyme, but significant amounts are adsorbed on the bacterial surface *in vivo*. When *H. pylori* is incubated *in vitro*, urease levels increase dramatically in the incubate. Urease production by the bacterium is controlled by nine genes clustered together on the *H. pylori* chromosome and code for assembly of the two basic subunit urease enzymes, insertion of a nickel ion and possibly transport of the active enzyme outside the cell. Urease is highly conserved, cross reacts with all Helicobacter species and is highly immunogenic- a property being exploited for use of urease as a vaccine antigen. Urease enzyme breaks urea into carbon dioxide and ammonia. The enzyme has a central role to play in the survival of the organism in an otherwise unfavorable acid medium of the stomach. Understandably, production of large amounts of ammonia does help the organism to neutralize the acid and maintain a film of friendly pH around it for survival. By doing so urease helps the organism to colonize on to the epithelium. In addition ammonia causes tissue damage and is involved in the pathogenesis of gastritis. Urease activity has been exploited in two main diagnostic tests for current infection of *H. pylori* namely rapid urease test and c^{13} or c^{14} urea breath test [24-27].

For *H. pylori* to live in its host, two phenomena namely colonization and induction of tissue injury are important [15]. For the organism to colonize, urease enzyme [23] and bacterial motility [28] are essential Urease protects organism from acid as elucidated earlier. Motility of *H. pylori* is achieved by sheathed flagellae, which allow the bacteria a burrowing movement into and through the gastric mucus to reach the epithelium. The bacteria adhere to the epithelium through adherence factors hemagglutinins, an intimin-like protein, Lewis blood group and an adhesion lipoprotein [29].

For inducing tissue injury, role of urease enzyme and ammonia related tissue injury has been elucidated earlier. Two proteins namely cytotoxin associated gene protein (cag-A protein) and vacuolating associated cytotoxin protein (vac A protein) play major role. These proteins are encoded by corresponding genes, the cagA gene and the vacA gene, both of these of these genes have been cloned and sequenced. CagA protein induces the secretion of

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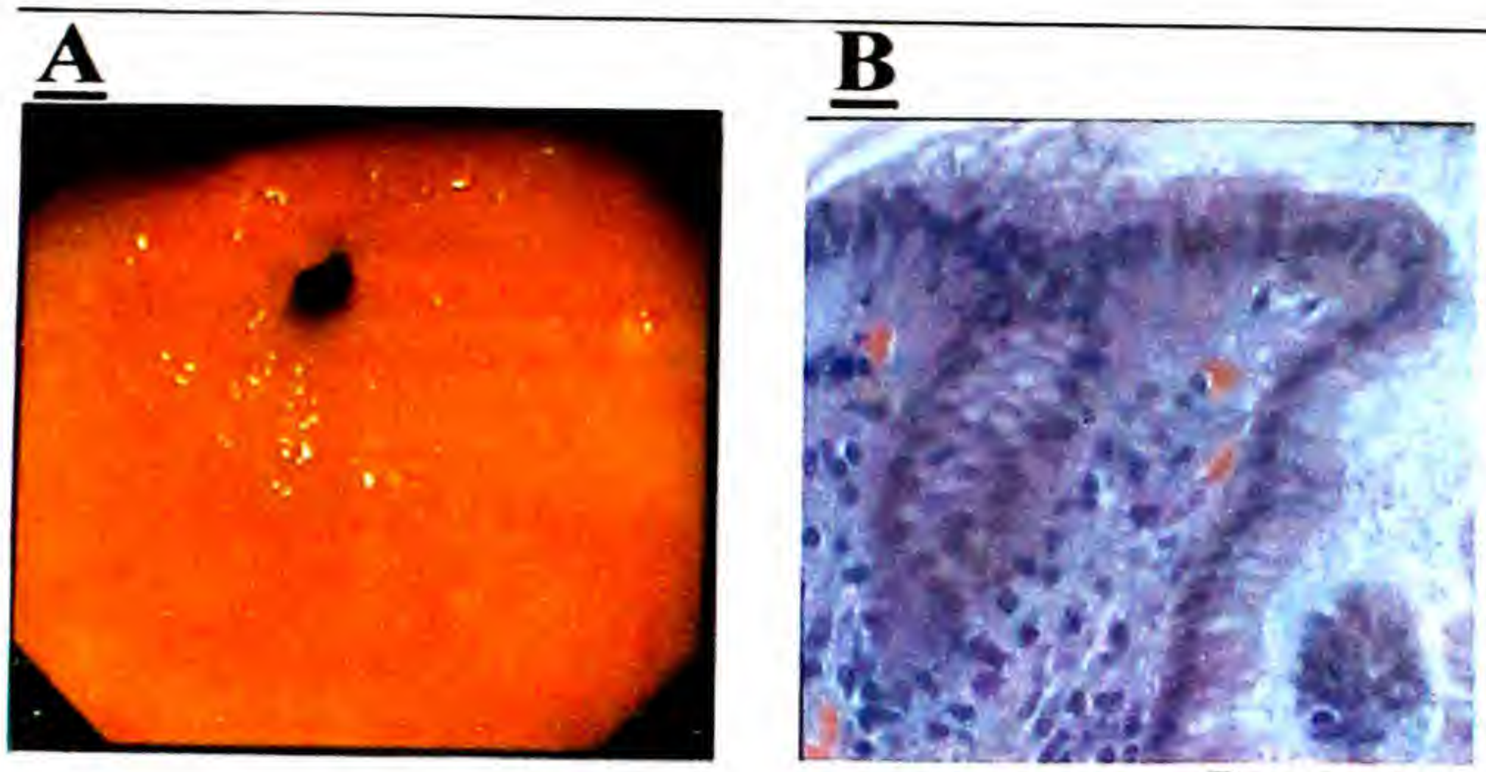

Fig 1. *Helicobacter pylori* habitat. A. Endoscopic photograph of gastric antrum revealing erythematous non-erosive gastritis of moderate severity , caused by H. pylori infection. B. Microphotograph of gastric biopsy showing numerous *H. pylori* organisms in the mucus layer of the epithelium of gastric mucosa.

cytokine interleukin-8, which recruits neutrophils leading to inflammatory response. Many studies from developed countries have found positive association of cagA $^{+}$ strains of *H. pylori* with duodenal ulcer, gastric atrophy, intestinal metaplasia, gastric cancer and MALT lymphoma. However studies from China and Japan have found high prevalence of cagA^{+} strains in both diseased states and control groups. On this basis, cagA positivity cannot be used as a marker for pathogenic strains of *H. pylori*. VacA protein has vacuolating cytopathic effects on several mammalian cell lines in tissue culture. All *H. pylori* strains carry a vacA gene. However, the gene is switched on in strains, which produce vacuolating toxic protein and switched off in those, which do not produce vacuolating toxic protein. The regulation of switch on and off phenomenon of vacA gene is poorly understood. *iceA* (*i*nduced *c*ontact *e*pithelium) gene, which is induced by contact with epithelium, has been recently identified. The gene product is unknown and is likely a bacterial restriction enzyme. Data on the disease property of this gene have shown that it has no role in H. pylori-related disease [30-34]

H pylori infection alters many aspects of gastric physiology. H pylori can both increase as well as decrease acid secretion, explaining the very varied clinical manifestations of H pylori infection. Hypergastrinemia is one of the consistent features, most likely caused by impairment of somatostatin secretion. In addition, H pylori is known to disrupt the gastric mucus layer. The effect of the organism on gastric motility abnormalities has not been conclusively established [15].

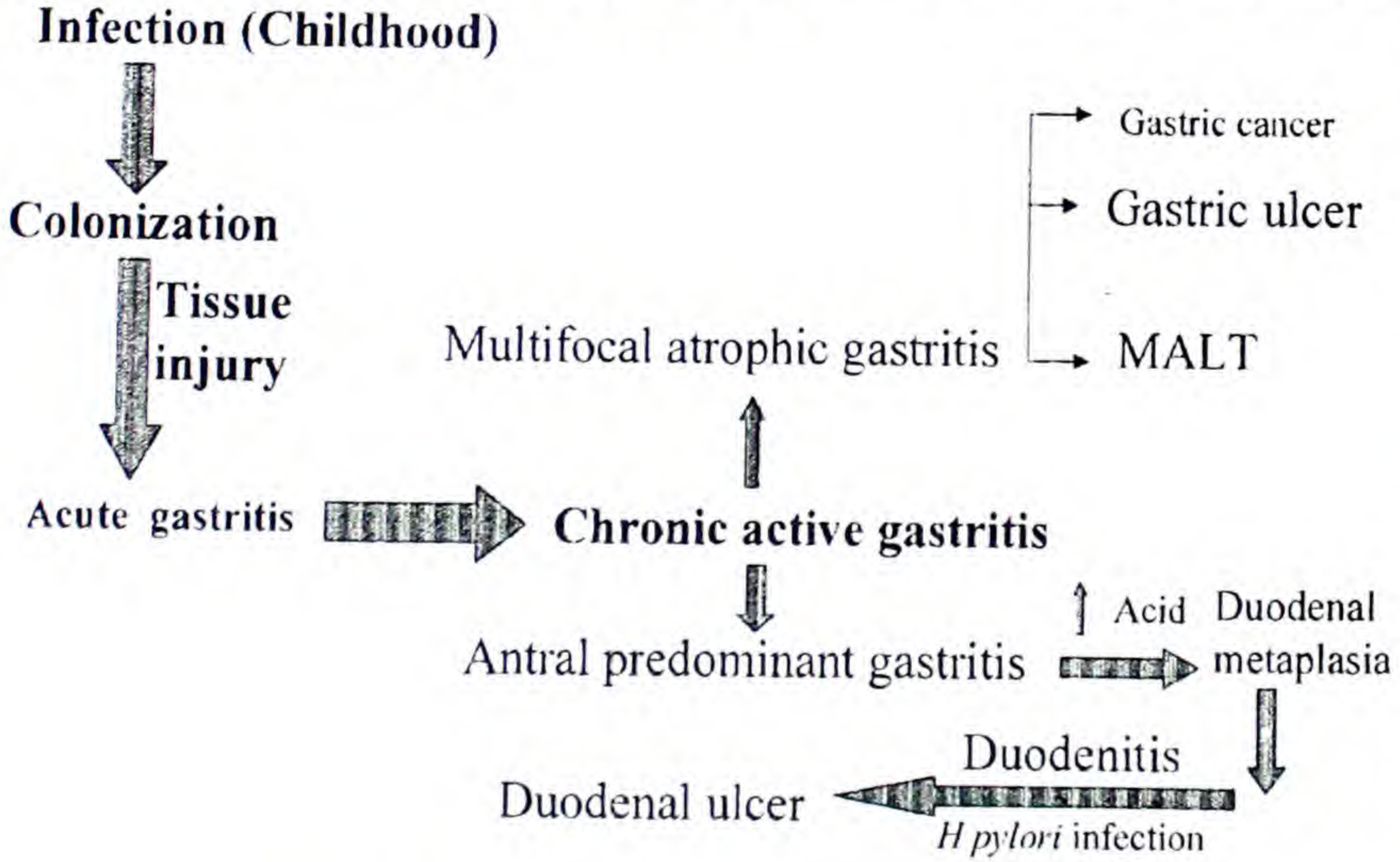

Fig 2. Natural course of Helicobacter pylori infection.

Genome

In 1997, the complete genomic sequence of *H. pylori* strain 26695 was published [35]. *H. pylori* has a circular genome with over 16 hundred thousand base pairs and 1590 predicted coding sequences. Sequence analysis indicates that *H. pylori* have a well-developed system for motility, for scavenging iron, and for DNA restriction and modification. Publication of the complete genomic

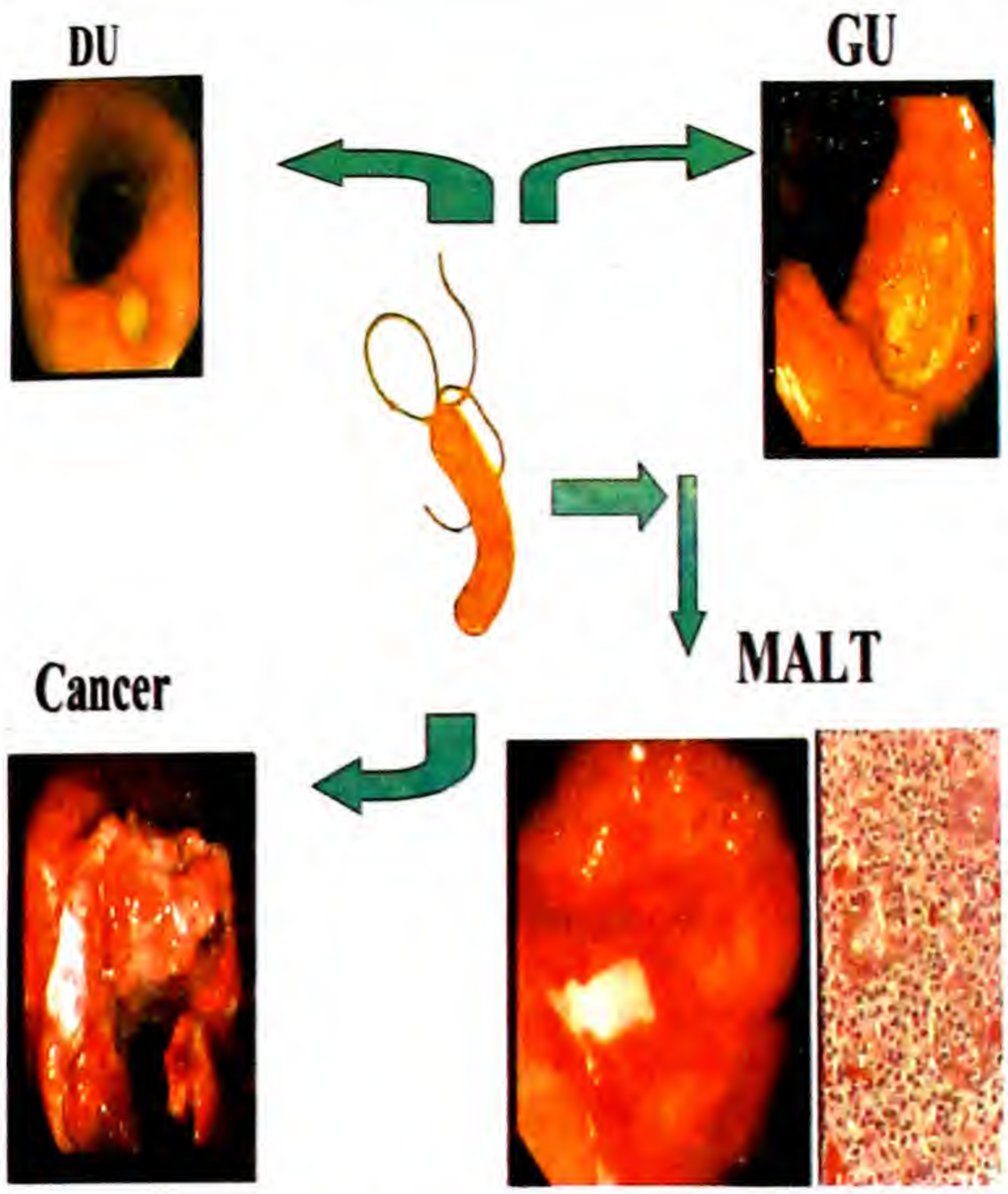

Fig 3. Cinical diseases caused by H. pylori. DU. Duodenal ulcer GU. Benign gastric ulcer. Cancer. Gastric cancer. MALT. Gastric MALT lymphoma with chronic gastric ulcer (left panel) & heavy lympho-plasmocytic infiltrate, centrocyte-like cells and destruction of the gastric glands- lymphoepithelial lesions (right panel).

sequence of *H. pylori* has marked the start of a new era of research into its role as a human pathogen.

Epidemiology

Understanding the epidemiology of *H. pylori* infection is an essential step in the development of public health measures. The studies performed on the prevalence of *H. pylori* infection in developing and developed countries have been a matter of intense debate and consequent to this, a model for *H. pylori* infection has been proposed . In this model, *H. pylori* proposed to be primarily a childhood infection globally, with little or no disease being acquired progressively in adulthood [39-41]. The age related prevalence of *H. pylori* from the developing countries fit this model very well. In these countries prevalence of infection is around 70 percent by 15 years of age, with no or little increase in prevalence rates above 30 years. The data from developed countries show a low prevalence (5-15 percent) of infection in childhood with moderately high prevalence (20-65 percent) in age group above 30 years . Such data could be interpreted in two ways: (1) *H. pylori* infection is acquired progressively throughout life; (2) infection is acquired in childhood, with a large decrease in the risk of infection along the generations- the so-called cohort phenomenon. Recent data generated from developed countries on this support that in fact *H. pylori* is primarily a childhood infection. Serum samples were available which had been collected at different times over a period of 30 years in a series of children and adults of various birth cohorts. All these samples were analyzed fro *H. pylori* antibodies. The results of this study showed that people of the same age born in different time periods do not have the same prevalence of infection. In fact young people born in earlier cohorts had a higher rate of infection than those of the same age born in recent cohorts [42].

Epidemiological data are convincing that *H. pylori* is transmitted as an enteric infection [41, 43-46]. Low socio-economic factors namely lack of education, poverty, overcrowding, poor sanitation and unsafe water supplies are high risk factors. Interfamilial spread of the infection has been well documented. Medical personal are high-risk groups and gastroenterologists have higher prevalence of infection when compared to their other medical colleagues [47-48].

Whether infection is transmitted through fecal-oral or oral-oral route is a matter of debate. To support the fecal oral transmission are the evidences that bacteria are excreted in feces alive, can survive in environment including water and have been shown to be transmitted through water and raw vegetables. Oral-oral transmission is supported by data that bacteria colonize oral cavity especially the dental plaques; infection can be transmitted by kissing and premastication of food by mothers to their babies; and cohabitating animals can transmit the disease through habit of extensive licking [49]. However, not all studies have shown evidence for oral-oral transmission of infection. Of significance is the data that dentists do not have higher prevalence of *H. pylori* infection, indicating that saliva is not a risk factor [50].

Non-human reservoirs for *H. pylori* have been suggested since the first description of the infection, but it is only recently that isolation of ***G***astric ***H***elicobacter-***L***ike ***O***rganisms (GHLOs) from the inflamed gastric mucosa of domestic cats and farmyard animals and ability to experimentally infect cats with *H. pylori* has raised the possibility of zoonotic infection. GHLOs, commonly noted in dogs and cats, are associated with approximately 0.08-1 percent of gastritis in humans. These GHLOs often infect patients who own pets, suggesting a zoonotic link [51].

The contamination of endoscopes and biopsy forceps with *H. pylori* occurs readily after endoscopic examination of *H. pylori* positive patients [52]. Unequivocal proof of iatrogenic transmission of the organism has been provided. **Endoscopic transmission of H pylori should be**

considered a possibility, although the magnitude of risk is largely unknown. Estimates for transmission frequency approximate to 4 per 1000 endoscopies when the infection rate in the endoscoped population is around 60 percent [53]. Endoscopic transmission of *H. pylori* produce what has been described by Japanese workers as post-endoscopic acute gastric mucosal lesions [54]. Traditional cleaning and alcohol rinsing is insufficient to eliminate endoscopiic / forceps transmission. Only meticulous adherence to disinfection recommendations guarantees *H. pylori* elimination. In a survey of 74 endoscopy centers in Western Europe 30 % inadequately disinfected endoscopes after procedures involving patients with upper gastrointestinal endoscopies and unknown HIV or HBV status. For routine procedures in patients with unknown HIV or HBV status, 70 % of centers did not adequately disinfect instruments after ERCP, 87% did not adequately disinfect instruments after colonoscopies, and 100% did not adequately disinfect instrument after upper endoscopies [55]. An Australian survey reported that only 45% of hospitals both cleaned and disinfected endoscopes satisfactorily. In a recent collaborative investigation of 26 health care facilities, investigators found that 78% of them failed to sterilize biopsy forceps; they isolated at least 100000 colonies of *H. pylori* or enteric bacteria from 25% of cultures taken from the internal channels of 71 endoscopes. Fundamental errors included respective failures to time the period of disinfection, to clean all channels, to flush all channels with disinfectant, to fully immerse the endoscope in the disinfectant solution, and to use a disinfectant. Automated endoscope washers are now widely available, but, are in use from 17% to 69 % of endoscopic centers in various countries [56] .

Natural course

Natural course of *H. pylori* infection in human has been well documented (Fig 2). *H. pylori* infection causes characteristic syndrome of acute gastritis, which regresses over a period of few weeks. Over 80% patients develop chronic infection of the stomach causing chronic active gastritis. This infection is a lifetime event in the natural setting with low rates of loss of infection. Majority of these patients are asymptomatic and this is how *H. pylori* survives in the host. In fact over 50% population of the world have this clinical setting. For reasons ill understood at present, a small group of individuals could fall into two alternative tracts. About 5-15% continue to have antral predominant gastritis with gastric hypersecretion and formation of duodenal ulcer. A smaller group shall develop syndrome of multifocal atrophic gastritis, which eventually ends up in one of the 3 disease states namely gastric ulcer, gastric cancer and MALT lymphoma. What host or agent factors determine *H. pylori* pathogenicity is under intense studies [15].

Acute infection with *H. pylori* gives rise to self-limiting upper abdominal symptoms, neutrophillic gastritis and reduction in the acid secretion lasting up-to 4 months. Persistent lifetime infection develops in over 80 % individuals. The organism selectively localizes in gastric antrum. All such subjects have chronic active gastritis in gastric antrum biopsies. This form of gastritis has 3 features namely focal epithelial damage, dense inflammatory infiltrate dominated by plasma cells with frequent lymphocytes and little or no neutrophils and lastly formation of lymphoid follicles with well developed germinal centers- the so called *M*ucosa *A*ssociated *L*ymphoid *T*issue (MALToma). *H. pylori* organisms can be seen in the mucus on the epithelial surface as curved spiral structures. As mentioned earlier, such patients are asymptomatic and no clinical syndrome has been attributed to this as of today [15,57].

Of great significance to pathogenicity of *H. pylori* is to understand the common topographical patterns of chronic gastritis. Acute infection causes acute neutrophillic gastritis involving the whole gastric mucosa. Chronic active gastritis involves antrum with sparing of the corpus of stomach (antral predominant gastritis). Both these types of gastritis do not cause atrophic changes in the gastric mucosa. Multifocal atrophic gastritis as the name suggests involves both corpus and antrum of stomach and is accompanied over the years by atrophy and intestinal metaplasia of gastric epithelium. Corpus predominant gastritis without involving the antrum is associated with pernicious anemia and has an autoimmune basis. This is not related to *H. pylori* and organisms are absent in this type of gastritis [57,58].

Clinical diseases

What are clinical outcomes of *H. pylori* infection. *H. pylori* is etiologically related to four gastro-duodenal diseases, which have been examined in detail (Fig 3). There is intense debate whether non-ulcer dyspepsia is or is not related totally or in part to underlying *H. pylori* infection.

There is unquestionable epidemiological evidence that most, if not all, of the duodenal ulcers are etiologically associated with *H. pylori* infection. Over 80-95% duodenal ulcer patients are infected with *H. pylori*. All case control studies have shown significantly higher prevalence of *H. pylori* in duodenal ulcer patients when compared to age and sex matched controls. Of significance is the data that *H. pylori* precedes development of duodenal ulcers. In well-done longitudinal studies patients chronically infected with *H. pylori* have three to fourfold risk of developing ulcer than those not infected. The final and most convincing proof that *H. pylori* is the key pathogen in peptic ulcer disease is the observation that eradication of *H. pylori* prevents ulcer relapses. Duodenal ulcers will relapse in around one half of patients after effective acid suppressant

therapy at one-year follow up and nearly invariably over long term follow up. Concomitant *H. pylori* eradication significantly reduces the ulcer recurrences to less than 10 percent at one year. With the exclusion of idiopathic ulceration in a small minority of patients, ulcer recurrence is generally only associated with *H. pylori* reinfection, or use of ulcerogenic drugs. Apart from defining cause and effect relationship, these data are of major clinical importance as ulcer disease can now be cured with a short course of antibiotics. This data truly define ulcer as an infectious disease rather than acid peptic disease-a doctrine we are preached for long [58-61].

Recent data have accumulated that patients with non-variceal gastro-intestinal bleeding significantly benefit in the long run by *H. pylori* eradication. Recurrences of gastro-duodenal bleeds are prevented over ensuing two to three years. Clinical experience has shown *H. pylori* eradication can promote healing of intractable non-healing or giant ulcers [62-63].

Several steps in the ulcerogenic pathway in *H. pylori* induced duodenal ulcer have been documented. *H. pylori* induces antral predominant chronic active gastritis. This leads to hypergastrinemia and fall in somatostatin secretion. With normal gastric corpus, both these hormonal changes cause gastric acid hypersecretion through stimulation and trophic changes on the parietal cell mass. Long- term acid hypersecretion causes gastric metaplasia of the duodenal bulb mucosa. Gastric metaplasia is a favorite site for *H. pylori* infection. This infection causes epithelial cell damage and duodenitis and duodenal erosions are produced. Duodenal erosions coalesce together to form duodenal ulcer[64-65].

H. pylori has since been defined by WHO as "class 1 carcinogen". The evidence that *H. pylori* infection is linked with the development of non-cardiac gastric adenocarcinoma comes from different aspects listed. There is direct strong association between sero-positivity of *H. pylori* and incidence and mortality from gastric adenocarcinoma in most regions of world. The EUROGAST study, one of the largest geographic studies of *H. pylori* and gastric carcinoma to date, gathered data from 17 populations in 11 European countries, the United States, and Japan. There was highly significant correlation between prevalence of *H. pylori* infection and gastric cancer incidence and mortality. The risk of gastric cancer was six times greater in *H. pylori* infected than in uninfected persons. However, one exception to this rule is "Indian-African enigma": the prevalence of infection being high in some regions where incidence of gastric cancer is low[66-71].

Excellent data from Finland have shown similar time trends in the incidence of gastric carcinoma and prevalence of *H. pylori* gastritis at age 50 years in different birth cohorts over last 100 years. These figures demonstrate that incidence of gastric cancer and the prevalence of *H. pylori* gastritis have been high at the same age in the cohorts born at the beginning of the century and low in those borne recently. A gradual decrease in the incidence of cancer and "birth cohort specific" prevalence of gastritis had occurred over time, the so-called cohort effect. Case control studies have demonstrated higher prevalence of *H. pylori* infection in patients with gastric cancer when compared with age and sex matched controls with an odds ratio of 3 to 4. Similar studies performed in patients with young ages have shown a higher risk with an odds ratio of 13. The etiological association of *H. pylori* with gastric cancer has been strongly supported by prospective cohort studies. Subjects infected with *H. pylori* had higher incidence of gastric cancer than controls with an extremely high odds ratio of 12.

The magnitude of increased cancer risk associated with H. pylori infection is substantial. Considering the above attributable risks, prevalence of H. pylori at 35 % in adults in developed countries and 85% in adults in developing countries, a minimum of 327,000 cases of gastric cancer per annum are being caused by H. pylori, although the number may be as high as 609,000.

Recently gastric adenocarcinoma has been induced in ferrets naturally infected with H. pylori by using a low dose of gastric carcinogen N-methyl-N-nitro-N-nitrosoguanidine.

Despite such an etiological association between H pylori and non-cardiac gastric adenocarcioma, eradication of H. pylori has not been shown as of today to reverse gastric atrophy, intestinal metaplasia and reduce the risk of gastric cancer. Data in this area are urgently needed in near future.

MALT lymphoma is a B-cell linage tumor, which occurs at a number of sites namely stomach, bronchus, thyroid, etc. All these sites lack lymphoid tissue and the disease starts by invasion of lymphoid tissue with lymphoid follicles at these sites. This stage is called MALToma. MALT lymphoma is diagnosed when lymphoid follicles are accompanied by a characteristic infiltrate made of centrocyte-like cells and plasma cells. However, hallmark of MALT lymphoma is occurrence of lympho-epithelial lesions, in which gastric glands are attacked and destroyed by the characteristic infiltrate [72-73].

The etiological association of H. pylori and gastric MALT lymphoma is stronger than gastric cancer. All such patients are infected with the organisms. In fact one of common histological features of H. pylori infection is induction of lymphoid follicles in the submucosa. H. pylori has been shown to stimulate B-cells in vitro. However the most convincing evidence comes form the data that low grade MALT lymphoma regress and are cured with eradication therapy. A number of long-term studies on large

cohort of patients have been published

One of the major contested issues in field of Helicobacteriology has been its relationship with non-ulcer dyspepsia. Let us start defining non-ulcer dyspepsia. It is defined as occurrence of persistent or recurrent epigastric pain or discomfort referred to upper abdomen lasting for a total cumulative duration of 3 months or more in the preceding 12 months. An upper gastrointestinal endoscopy is necessary to exclude an organic gastro-duodenal disease including duodenal ulcer, gastric ulcer and gastric neoplasm. Endoscopic and histological erythematous or erosive gastritis does not qualify an organic disease for this definition. Such findings are seen in patients with non-ulcer dyspepsia and asymptomatic matched controls in equal numbers and severity excluding their potential as an organic disorder and to explain such symptoms. However, two patterns of symptoms must be excluded while defining non-ulcer dyspepsia. Heartburn is a specific symptom pointing to gastro-esophageal reflux disease (GERD), which has well known pathogenesis, course and therapy. Majority of patients with have normal esophago-gastro-duodenoscopy (endoscopy negative GERD) and only a careful history is crucial in differentiating the two disorders. Patients with abdominal symptom related to bowel motions point to colonic disorder and are commonly seen in patients with irritable bowel syndrome [74].

Clinicians have a fashion to discover overlap syndromes and here also we are no exception. This slide depicts how these three group of symptoms namely heartburn, dyspepsia and colonic symptoms occur in the community. A sizable percentage has two or all the three groups of symptoms and patients can shift their description of symptoms from one to another over time periods. A good bed size clinician uses rule of dominance to decide on future course of action. Patients with non-ulcer dyspepsia have been subclassified into those with epigastric pain (ulcer type) and with distension (dysmotility type). Such a classification may help to target selective therapy (anti-ulcer for ulcer type and prokinetics for dysmotility type), however, the two groups cannot be differentiated on basis of pathogenesis and disease course [75].

How common is non-ulcer dyspepsia in the community? Non-ulcer dyspepsia is a common disorder and demonstrates a dynamic behavior. Well-conducted community studies have estimated prevalence of such symptoms varying from 14 to 26 percent. Incidence of the disease varies from 1 to 8 percent per year. About a third lose their symptoms per year. The severity of symptoms varies widely and only one fourth would have sought medical advice at any given time [76].

Does H. pylori infection cause non-ulcer dyspepsia? We do not know the answer as of today. Well conducted interventional studies have shown conflicting results and future work in this field shall be watched with great interest. Till then what does the clinician do with management of such a common disorder? I believe we should be guided by following data. Fifty percent of non-ulcer dyspepsia patients are infected with H. pylori (i.e. similar to that of the general population). If not treated around 5 to 15 percent of such patients have life time risk to develop duodenal ulcer as against no risk to patients with eradicated or no H. pylori infection. A small but definite risk of gastric cancer and MALT lymphoma does exist in infected patients. Eradication therapy shall give symptom benefit at one year to 35 percent of patients as against 28 percent on placebo. This treatment advantage of 7 percent is small and number to treat in order to cure one patient is 15. Well-done cost effective studies have shown that eradication of H. pylori is cost effective when compared to long-term anti-ulcer therapy. Personally I test and treat all patients of on-ulcer dyspepsia for H. pylori infection [77].

Diagnosis

H. pylori diagnosis has well-established diagnostic tools. Rapid urease test and histological examination of gastric biopsies for *H. pylori* organisms are gold standards at endoscopy. *H. pylori* culture is recommended only when first line therapy fails to eradicate the infection. Antibiotic sensitivity shall guide therapy in such patients. PCR is at present employed only as a research tool and can help in studying epidemiology of the organism and control of *H. pylori* transmission [24-27,79-81].

C^{13} or C^{14} Urea breath test is a global test for *H. pylori* infection with high sensitivity and specificity. The test is best used to confirm eradication after treatment. Rapid urease test and histology of gastric biopsies have limitation under this setting, due to reduced load of bacteria and are not recommended. As the test is non-invasive, sensitive and specific it is increasingly being used as the first line diagnostic test in patients not undergoing upper endoscopy. The only limitation is limited availability of this test in the institutional setting. Recent introduction of office type equipment to test for C^{13} urea breath test may obviate this difficulty [24-27].

Serological test are easy to perform but have limitation because these cannot differentiate current from past infection and test become negative after many months after eradication. However, these tests have immensely helped in the understanding of epidemiology and natural course of disease [82].

Who should be tested and treated for H. pylori (Table 1)[83-84]? All those conditions, which derive potential clinical benefit with H. pylori eradication, need the test. All uncomplicated duodenal ulcer have a distinct advantage with therapy as ulcer relapses are eliminated. H. pylori eradication in this setting is cost effective when compared

to long term H_2 antagonist therapy. Gastric ulcers can be broadly classified into 2 groups depending upon the etiology namely non-steroidal anti-inflammatory drugs (NSAID) and H. pylori. Should NSAID induced gastric ulcers be tested and treated for concomitant H. pylori infection? The mechanisms of peptic ulcer formation caused by H. pylori and NSAIDs are contrasting. H. pylori causes cytotoxin induced inflammation and ulceration while NSAIDs cause reduced prostaglandins and direct toxic effect on the gastric mucosa. There is no evidence of synergy between these two etiological agents. H. pylori eradication does not alter the relapse pattern of gastric ulcers with continued use of NSAIDs during 6-month follow-up period. Results on the effect and eradication of concomitant H. pylori in patients with no underlying ulcers and on long term NSAID therapy and are conflicting. Thus as of today there is no strong evidence to treat or prevent NSAID induced gastric ulcers by concomitant H. pylori therapy [85,86].

Patients with non-variceal upper gastrointestinal bleeding should be tested and treated for H. pylori infection. Apart from preventing relapses it prevents long-term ulcer complications over ensuing 2 to 3 years. MALT lymphomas are invariably H. pylori positive and low-grade gastric MALT lymphoma regresses with H. pylori eradication therapy. Long-term emissions and cures have been well documented.

Majority of the clinicians do test and treat H. pylori infection in patients presenting with non-ulcer dyspepsia. The evidence for and against has been presented.

How should the diagnostic tests be used judiciously in various clinical setting? Patients with suspected ulcer disease and no prior treatment need an upper endoscopy and rapid urease test and histological examination of gastric biopsies is ideal for this group of patients. Unless the ulcer disease is complicated or life threatening, there is no need to check for eradication of H. pylori [27].

If H. pylori eradication is to be confirmed after treatment C^{13} or C^{14} urea breath test has distinct advantage of being a global test and has good sensitivity under these circumstances. Negative urea breath test indicates cure. Patients with positive test need an upper endoscopy and gastric biopsies. Gastric biopsies must be cultured and antibiotic sensitivity defined to choose proper drug combination therapy. Unfortunately this can only be done in a tertiary care setting due to inherent problems in culturing H. pylori.

As dyspepsia is a common primary care problem and access to endoscopy is limited to gastroenterology practice, many primary health care services have adopted a test and treat policy for dyspepsia. In this only a small high-risk group (gastric neoplasm) of newly diagnosed cases of dyspepsia are referred for upper endoscopy. This group is identified by age and seven alarm symptoms namely weight loss (>3 kg in last 3 months), anemia, dysphagia, abdominal mass, GI bleed, family history of gastric cancer and anorexia/ vomiting. All other patients are offered a non-invasive test for H. pylori, either urea breath test or serological test for H. pylori antibodies. Patients with evidence of infection are treated for H. pylori and those with negative test receive empirical treatment. Patients with continued or recurrent symptoms at 12 weeks are offered an upper endoscopy. Test and treat policy has been found to be safe and cost effective in many health care delivery systems with low prevalence of upper GI cancers [74].

Treatment

H. pylori eradication therapy is a matter of continuing debate. The number and type of combinations are innumerable. The data accumulated in this area is a matter of much confusion fro a practitioner faced with such a common problem. However in all this there is lot of sense behind and while using this therapy we need to stick to rules of the game. First rule is not to use a single agent for treatment. All single agents have given eradication rates below 50 percent and are not acceptable in clinical management. Second rule is to use a strong acid suppressant drug along with antibiotic combination. Hypochlorhydria during antibiotic therapy enhances *H. pylori* eradication rates. Of great importance are the data that strong acid suppressant therapy, particularly with proton pump inhibitors (PPIs), overcomes resistance to metronidazole and possibly other antibiotics. Thirdly, antibiotic sensitivity pattern of H. pylori in the geographical region of practice needs to be kept in mind [87-98].

Overt the years the two combinations, which have shown consistently high eradication rates are shown. Most European studies use one-week triple therapy while North American studies use two-week therapy for high eradication rates.

A recently introduced combination named popularly the RBC based triple therapy combines ranitidine and bismuth and two antibiotics namely clarithromycin and amoxicillin. This combination has given consistently high eradication rate comparable to standard triple therapy (Table 2).

Antibiotic resistance to H. pylori is a problem, which shall become of great significance in future. As of today metronidazole resistance is seen in a high percentage of patients particularly developing countries. Clarithromycin resistance occurs from one to 12 percent of patients and amoxicillin resistance is rare.

Is antibiotic resistance of clinical importance as of today. I believe it is. Data show that when there is no resistance, eradication rates approach 100 percent. When there is resistance to one antibiotic, the risk of treatment failure increases, but eradication rates remain high and clinically acceptable. Resistance to two agents drops the eradication

rate to less than 50 percent. Of significance are the data that PPI therapy does overcome high degree resistance to metronidazole and clarithromycin. Metronidazole resistance is defined as minimal inhibitory concentration (MIC) of 8ug/ml o more. However, there is no clear association between resistance and treatment failures until MIC is above 32 ug/ml. Clarithromycin resistance is defined as MIC of 1 ug/ml or more. Treatment failures occur only when clarithromycin resistance reaches high grade with MIC of 128 ug/ml [87].

The high prevalence of Helicobacter pylori infection in the world, its implications in the appearance of gastric malignancies and the emergence of antibiotic resistance demand that prophylactic and new measures are developed against this infection. Two types of oral vaccines are being intensely under study. Candidate preventive vaccines include crude sonicates of Helicobacter felis and recombinant subunits of enzyme urease and catalase. A human vaccine using urease and heat labile enterotoxin of E. coli is already under field trial. Candidate treatment vaccine has had success in infected mice and clears the infection by hosting an immune response. The oral antigens used in these two types of vaccines have been shown to result in T-helper cell-2 driven immune response, which in turn stimulates B-lymphocytes. Natural immunity to H. pylori in contrast is a T-helper-1 driven response, which has no value in clearing or preventing the infection [99-100].

H pylori status in the Middle East

The prevalence of *H pylori* in the Middle Eastern population is around 60 %. The epidemiology of the infection in this region resembles to those of many other developing countries [101]. Of significance is the data that standard PPI-based triple therapy for one or two weeks gives *H pylori* eradication rate of 65 % at best. This low eradication rate was exclusively related to high-percent and high-grade resistance to first line antibiotics used in the therapy (Fig 5). In view of the above newer drug combinations need to be explored for H pylori eradication therapy in this region [102].

Table 1. Indications for *H pylori* eradication therapy

Recommendation *	*Clinical disease*	*Scientific evidence* **
Strongly recommended	Peptic ulcer disease (active or healed)	1
	Bleeding peptic ulcer	1
	Low grade MALT lymphoma	2
	Gastritis with severe abnormalities	2
	Post gastric cancer resection	3
Advisable	Functional dyspepsia	2
	Family history of gastric cancer	3
	Long term treatment with PPI for GERD	3
	Planned or existing NSAID therapy	2
	Following gastric surgery for peptic ulcer	3
	Patient's wishes	4
Uncertain	Prevention of gastric cancer	5
	Asymptomatic subjects	5
	Extra-alimentary disease	5

The Maastricht 2-2000 Consensus Report for eradication of H. pylori were recommended at 3 levels (* strongly recommended, Advisable & Uncertain) and these recommendations were evidence –based at 5 levels {**). 1. Well-designed and appropriately controlled studies; 2. Well-designed cohort or case-controlled studies, with persuasive indirect evidence; 3. Case reports, with suggestive indirect evidence; 4. Clinical experience; 5. Insufficient experience to form an opinion.}

Table 2. Recommended treatment regimens for *H. pylori* eradication

	Regimen 1	**Regimen 2**	**Regimen 3**
Type of therapy	PPI-based triple therapy	RBC-based triple therapy	Quadruple therapy
Drug/dose	PPI*(Standard dose) BID		
	Clarithromycin 500 mg BID		
	Amoxicillinb 1000 mg BID	RBCf 400mg BID	
	Clarithromycin 500 mg BID		
	Amoxicillinb 1000 mg BID	PPI* (standard dose) BID	
	Bismuth subcitrate 120 mg QID		
	Metronidazole 500 mg TID		
	Tetracycline 500 mg QID		
Duration	One / two weeksd	One / two weeksdOne week	
Status	First line therapy	First line therapy	Second line therapy

* Standard dose of PPI include Omeprazole 20 mg, lansoprazole 30 mg, pantoprazole 40 mg and esomeprazole (Nexium®) 20 mg given orally twice daily

f Ranitidine Bismuth Citrate

b Amoxicillin can be substituted by metronidazole in penicillin allergic patients,

d Maastricht Consensus Report 2-2000 recommends one-week therapy, while two weeks therapy is recommended by American Digestive Disease Foundation and approved by FDA

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OBITUARY

Professor Subhash R Naik 1943-2002

Prof. S. R. Naik passed away on the doctor's day (July 1, 2002). He was suffering from stomach cancer. At the time of his death Dr. Subhash was serving as Prof. & Head of the Gastroenterology Department at the Sanjay Gandhi Institute of Medical Sciences, Lucknow. In more than 30 years of illustrative research career Prof. Naik worked on various aspects of gastroenterology. Be it tropical problems or solving the mysteries of hepatitis B or hepatitis E viruses, Dr. Naik is credited with more than 200 original scientific papers.

Prof. Naik was born in August 1943 at Goa. He obtained his MBBS degree and post graduation from Maulana Azad College New Delhi. Moving from PGI Chandigah to King Edward Memorial Hospital Mumbai and finally to Lucknow he left his mark everywhere. Within 10 years of establishing the department of gastroenterology at Lucknow it was awarded the prestigious Pfizer Amir Chand Trophy of the Indian Society of Gastroenterology.

Prof. Naik was also the editor of the Indian Journal of Gastroenterology (IJG) for many years.

I had many interactions with him particularly during his visits to the SK Institute of Medical Sciences, Soura Srinagar which he visited in connection with selection and other related matters. He was a scientist pure and sure and his loss is a sad blow to the doctors, particularly the gastroenterologists. His contributions to the field of gastroenterology can not be side lined. Being an editor myself I can imagine how much extra hard work he must have put in at the IJG.

I as the president of IMA (Kashmir Branch) together with my colleagues at the Department of Gastroenterology, GMC, Srinagar and the staff of JK Practitioner convey our condolences to the bereaved family. May his soul rest in peace.

Prof. GM Malik
Editor JK Practitioner
President IMA, Kashmir Branch.
Head Division of Gastroenterology, GMC, Srinagar.

CONFERENCE CALENDER

LAPARO UPDATE 2002
CME and Live International Operative Workshop organised by Govt. Medical College Srinagar, Kashmir & Medical Council of India. **Oct. 25-26, 2002** at SKICC and SMHS Hospital, Srinagar, Kashmir for details contact: Prof. Muneer Khan Organising Secretary, P.O. Box: 1216 GPO, Srinagar. E-mail: drmuneer123@hotmail.com.

6th Annual Meeting of the Indian Association of Cardiovascular and thoracic Anaesthesiologists, 8th - 10 Nov. at Lucknow. For details contact organising Secretary Dr. Prahabat Tewiri Tele: 0522-440700/ 24-29 Fax: 0522-40001 E-mail ptewari@satyam.net.in

XXXIII Annual Conference of the Indian Society of Nephrology, 15-17 Nov. at Jaipur for Details contact Organising Secretary Dr. S K Pareek Tele: 0141-61800, 602525 (R), 560291 ext. 561 (H)
E-mail: isncon2002@datainfosys.net.

Microsurgery Training Workshop (for fallopian tube & vas recanalisation Organised by the Family Welfare Association of India Mumbai, **18-22nd Nov.** 2002 Details Tele: 022-2029080/2025174 Fax: 022-2029038/2048513. E-mail: fpai@gaisbm01.vsnl.net.in.

The VI International Surgical Conference of the Society of Surgeons of Nepal will be held at Kathmandu, Nepal, Nov. 21-23 2002. Organising Secretary Dr. Manohar Lal Shrestha E-mail: ssn@healthnet.org.np. Fax: 997(1) 225300.

NAPCON 2002-4th National Conference of Pulmonary Diseases under the auspicious of National College of Chest Physicians of India and Indian Chest Society, 20-24th Nov. at Jaipur. Details Organising Secretary Dr. Nirmal Kumar Jain tele. 0141-304348 (R) 340414 (H)
E-mail: napcon@indiatimes.com

24th National Conference of the Association of Radiation Oncologists of India (AROI) Organised by AROI Karnataka chapter 21-24th Nov. at Bangalore. Contact Dr. Ramesh S Bilimagga Tele: 080-293862

2nd SIOP (International Society of Pediatric Oncology) – Asia Conference and 6th Annual Conference of Pediatric Hematology Oncology, 22 to 24 November at New Delhi. For details contact Organising Secretary, Dr. L. S. Arya, Department of Pediatrics, Division of Pediatric Oncology All India Institute of Medical Science, New Delhi-110 029. Tel.: 011-659 4610, 659 3209, fax: 011-686 2662; email: lsarya@rediffmail.com;
website: www.SIOPPasia2002.com.

Answer to the Photo Quiz Page 269

A. Unilaterla Clubbing of the right middle finger.
B. Trauma

Editor's Diary

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1. Prof GM Malik (President IMA State Branch) receiving an award from Mr. Nanda Secretray Family Welfare. Ministry of Health, during Academia 2001 at Asholka Hotel, New Delhi in recognition of services rendered.

2. In conversation Prof. Okhda renowned hepatologist with Prof GM Malik during ISG Conference at New Delhi 2000.

3. Annual Conference of Indian Society of Gastroenterology New Delhi 2000. Prof Goyal (Ex. Chief Editor American Journal of Gastroenterology USA) with Prof. GM Malik also seen are Dr. Kotwal, Governor American College of Gastroentrology, India), Dr. Javid and Jaswinder Singh are seen at the extreme.

4. Prof. GM Malik, President Medical Faculty Association (MFA) being honoured by Mian Altaf Ahmad Hon. Minister of Health and Family Welfare, Govt. of J&K Dr MA Qazi Gen Secretary (MFA) is seen in the centre.

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